ITERIM SESSION—ST. LOUIS, NOV. 30-DEC. 3, 1948
NUAL SESSION—ATLANTIC CITY, JUNE 6-10, 1949

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THE JOURNAL

OF THE

American Medical Association

Subscription, $12.00 | Published Weekly at | *Single Copy*, 35 Cents
VOLUME 138, No. 13 | 535 North Dearborn Street, Chicago 10, Illinois | NOVEMBER 27, 1948

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $12.00 a year, 25c a copy. Canadian $13.50. Foreign $16.00. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under act of March 3, 1879. Address all communications to American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois.

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 138, No. 13 — CHICAGO, ILLINOIS — NOVEMBER 27, 1948

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A PRESENT DAY RATIONALE FOR THE TREATMENT OF URINARY TUBERCULOSIS

Chairman's Address

REED M. NESBIT, M.D.
and
A. WAITE BOHNE, M.D.
Ann Arbor, Mich.

Streptomycin has been demonstrated to be effective in the treatment of many types of urinary tuberculosis, with the result that a new and hopeful attitude regarding the prognosis of the disease prevails. But new discoveries are often accepted and utilized by the public without an adequate orientation in thinking regarding the ultimate changes which may be brought about by the new agency. An example in point is modern air transportation. The public knows that our continent can be spanned by air in one day; yet New York and San Francisco are still five days apart in the thinking of most persons because of our orientation to earth-bound travel. The present discussion is related to a reorientation of our thinking in the matter of treating urinary tuberculosis; for it is now evident that we should treat all patients with this disease by prolonged sanatorium care and streptomycin therapy whether the infection appears to be clinically bilateral or unilateral, and the following evidence is presented in support of this view.

Urologists have generally agreed that unilateral caseating renal tuberculosis does not heal spontaneously and, for this reason, have always advocated nephrectomy in its treatment. Likewise it is known that the prognosis in bilateral renal tuberculosis is poor, although there are several reports in the literature enumerating patients with bilateral disease who have survived for remarkably long periods of time.

Most urologists today are using streptomycin in treating urinary tuberculosis. There is a unanimity of opinion regarding the general effectiveness of this form of treatment, but time and experience are as yet lacking for an adequate evaluation of the method. Therefore, the precise indications for its use, the exact dosage and the optimal duration of treatment are yet to be disclosed by experience. How soon these factors can be determined is a matter of conjecture. The Veterans Administration is attempting to determine the optimal dosage, duration of treatment and method by observing large groups of patients treated by various plans of streptomycin administration; but even under the controlled conditions that prevail in this large scale study the final results will be long in appearing and will be related largely to a special group of patients—young male subjects.

The urologist today properly wonders how he should approach the matter of planning a course of treatment in any case of urogenital tuberculosis. His indecision is obviously not concerned with the treatment of frank bilateral disease, for there are no alternate methods in that situation. Streptomycin offers the only hope of suppressing the disease in such a circumstance. His concern is related rather to deciding between alternate regimens when he is confronted by a patient with unilateral infection. It is the purpose of the present inquiry to discuss the rationale of streptomycin therapy in the management of unilateral renal tuberculosis. Our investigation must include an evaluation of three important factors that have a significant bearing on the problem: (1) the effectiveness of streptomycin in the healing of tuberculous lesions in the urogenital tract and the risks inherent in streptomycin therapy, (2) the pathologic aspects of the disease and (3) the prognosis of patients who are treated for unilateral disease by nephrectomy alone.

EFFECTIVENESS OF STREPTOMYCIN IN TUBERCULOUS LESIONS IN THE UROGENITAL TRACT; RISKS OF TREATMENT

Most investigators agree that streptomycin will cause an arrest or an improvement in the majority of the tuberculous lesions that occur in the urinary tract. At the present time the best results appear to have been attained in two groups of cases: (1) those having residual cystitis following nephrectomy for clinically unilateral disease and (2) those who have lesions of one or both kidneys which can be diagnosed by the observation of tubercle bacilli and pus in the urine obtained by ureteral catheterization, but which show no roentgen evidence of destruction in the kidney. Recently Lattimer and others [1] asserted that only renal lesions of this type have responded favorably to streptomycin therapy. These investigators have had a large experience in the antibiotic therapy of urogenital tuberculosis, and their opinions, which are based on accurate and exhaustive case studies, may be looked on with respect. The experience of these authors, however large, is limited, and their declarations that advanced renal lesions—i. e., lesions which are visible in the pyelogram—will not become arrested by means of streptomycin therapy, cannot be regarded as final or determinative. There are already several reports from competent and reliable observers enumerating cases of this type, in which there was healing under antibiotic treatment and the patients remained free from

From the Department of Surgery, University of Michigan Medical School, Ann Arbor, Mich.

Read before the Section on Urology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948.

1. Lattimer, J. K., and others: Streptomycin in Treatment of Genito-Urinary Tuberculosis, J. Urol., to be published.

pus and tubercle bacilli for long periods of time. A case in point is one which we now have under our observation in the clinic of the University of Michigan Hospital (case report).

L. W., a 22 year old woman, had suffered from moderately advanced bilateral pulmonary tuberculosis for four years, which was complicated by tuberculous peritonitis in 1946. At that

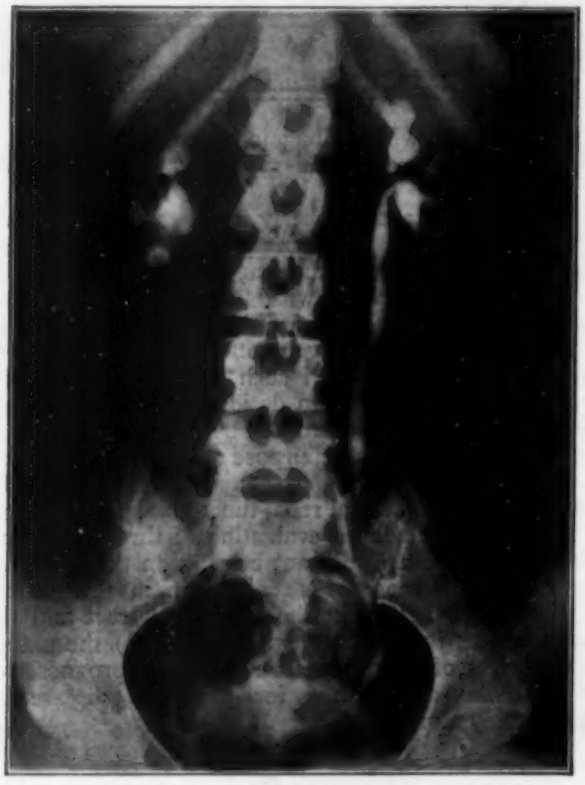

Fig. 1.—Pyelogram prior to streptomycin therapy.

time asymptomatic pyuria developed, which prompted an investigation of the urinary tract, and bilateral destructive renal lesions were demonstrated. Streptomycin therapy was begun in June 1947, 1.5 Gm. per day being given for seventy days while she remained in the sanatorium. The urine became free from pus and organisms after streptomycin therapy and had remained free from all evidences of infection after twelve months. Ninety days after streptomycin treatment was begun the patient was found to have a ureteral stricture at the bladder level on the right, and also evidence of a massive cicatrix in the left kidney which appeared to threaten its survival. A right cutaneous ureterectomy was performed in October 1947, and the patient was clinically well as of the date of writing. Pyelographic examinations in May 1948 revealed no abnormalities on the right side as well as a remarkable improvement of the left kidney, and the urine was still free from pus or tubercle bacilli that could be demonstrated by all methods of identification.

Final opinions regarding the optimal streptomycin dosage and the duration of treatment must be delayed until adequate data have accumulated. At the present time there appears to be a tendency toward the favoring of smaller dosages than those originally employed. Among the reasons for this attitude are the factors of expense and the avoidance of toxicity. Neither of these items should be regarded as extravagant when the suppression of a lethal disease is the object of the expenditure. At the present moment the evidence in favor of a dose smaller than 2 Gm. per day in the control of urinary tuberculosis is at best tenuous, if not completely lacking. In our own small series of 29 cases that have been followed up sufficiently long for significant observation, it has been interesting to note that the only failures or relapses have occurred in patients who were treated with doses of streptomycin that were less than 2 Gm. per day. To be sure, most of the patients have suffered some loss of vestibular function, and a few have demonstrated impairment of hearing, but they are alive and, although a bit wobbly, are all enjoying remissions, and we and they are content with the outcome.

PATHOLOGIC ASPECTS OF THE DISEASE

Any rationale for the treatment of disease must be predicated on a basic understanding of its pathologic aspects. This is particularly true of urinary tuberculosis, which is a metastatic disease, and the blood-borne organisms are invariably deposited in both kidneys as well as in other tissues of the body. The classic study of Harris [2] demonstrated that tuberculosis of the urinary tract occurred frequently among tuberculous children who had bone involvement but rarely among children who had only pulmonary lesions. Conclusive evidence regarding the universal bilaterality of the disease was furnished by the monumental studies of Medlar [3] in 1926. This investigator examined serial sections of the kidneys from persons who had died of pulmonary tuberculosis and found that bilateral cortical infections were present in all the kidneys. The majority of the lesions were minimal in size and showed evidences of healing.

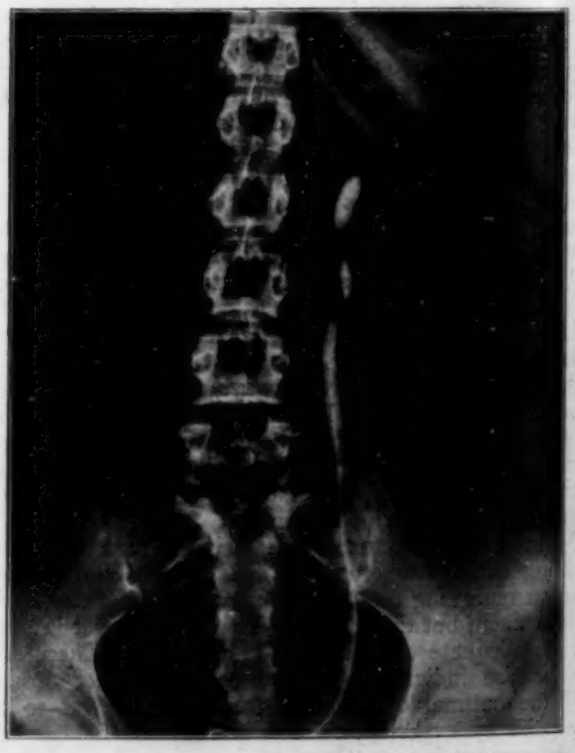

Fig. 2.—Retrograde pyelograde pyelogram (left) after streptomycin therapy, disclosing constriction of the pelvis. (The urine was normal.)

Only a few of the hundred and fifty thousand sections that he studied showed lesions that the clinician might be able to demonstrate by pyelography. Yet all the kidneys were doubtless capable of producing tuberculous

2. Harris, R. J.: Tuberculous Bacilluria: Its Incidence and Significance in Patients Suffering from Surgical Tuberculosis, Brit. J. Surg. **16**: 464-484, 1929.

3. Medlar, M.: Renal Infection in Pulmonary Tuberculosis; Evidence of Healed Tuberculous Lesions, Am. J. Path. **2**: 401-413, 1926.

bacilluria. Additional data relating to this subject have been recently provided by this same pathologist. At the Boston meeting of the American Urological Association in May of this year (1948) Dr. Medlar read a report entitled "Post Mortem Compared with Clinical Diagnosis of Genito-Urinary Tuberculosis in Adult

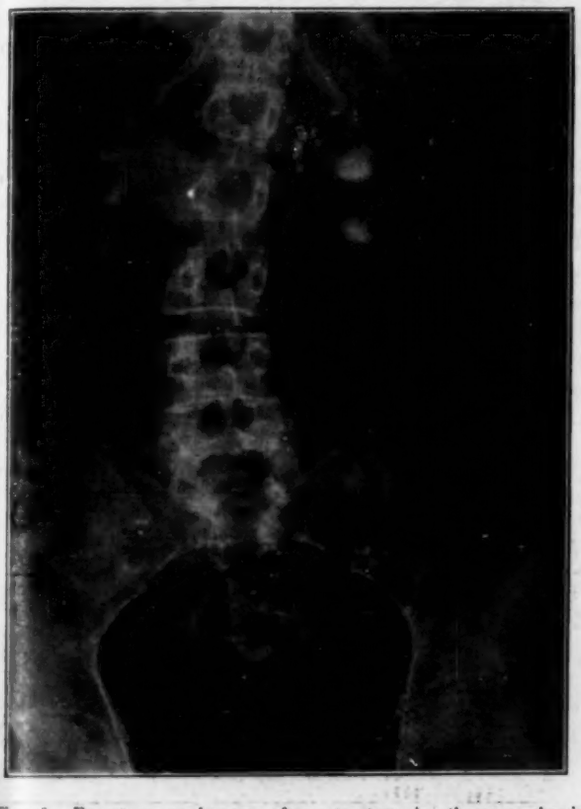

Fig. 3.—Excretory pyelogram after streptomycin therapy, showing dilatation of the left side of the pelvis above the constrictive lesion.

Males."[4] His observations were based on 5,424 necropsies performed on male subjects over 16 years of age at Bellevue Hospital. He found that nearly all renal infections were bilateral and that other organs of the urogenital tract invariably were involved. One of his conclusions based on this study was:

> The clinical management of a patient with genito-urinary tuberculosis should be based upon a clear concept of the pathogenesis of tuberculosis as a whole. If the intention is to prevent a further spread of the disease within the system by surgical removal of the organ in which tuberculosis is recognized, the data presented in this paper indicate that already other organs are affected and the surgical procedure is too late to obtain the desired results.

PROGNOSIS WITH NEPHRECTOMY ALONE FOR CLINICALLY UNILATERAL DISEASE

Another factor which must be considered in viewing the present problem is that which relates to the prognosis following nephrectomy for clinically unilateral disease. This important facet of the picture is one that unfortunately has received only scant attention by urologists in the past. To be sure, there is an extensive literature devoted to the discussion of various other aspects of the problem, and there has been a wide acceptance of the doctrine that nephrectomy is indicated in patients who are demonstrated clinically to have tuberculosis confined to one kidney. The clinician has perhaps been forced to depend on the implication that when the disease was properly diagnosed and appropriately treated the patient got well, for he has been told repeatedly that nephrectomy must be performed if the patient is to recover; but analyses of the results of nephrectomy have been conspicuously lacking in the literature. An outstanding contribution in this regard is that which was reported by Wildbolz[5] of Switzerland in 1925. Wildbolz reported that 59 per cent of his nephrectomized patients became cured after operation, the majority of the remaining patients dying of renal or some other form of tuberculosis. There have been only three series of cases reported in this country which can be utilized in deriving conclusions regarding the value of nephrectomy: that of Giles[6] in 1937, dealing with 96 patients operated on at the Squier Clinic; the Mayo Clinic series of 1,131 patients reported by Emmett and Kibler[7] in 1938, and 153 cases that were reported by Nesbit, Keitzer and Lynn[8] in 1945. These three series of cases provide an aggregate of 1,380 patients who were treated in recognized clinics and in whom the criteria for operation were such that a reasonable expectation for cure must have prevailed at the time that nephrectomy was performed. Yet only about half of

Fig. 4.—Pyelogram made one year after streptomycin therapy and seven months after right cutaneous ureterostomy, with apparent regression of the constrictive lesion on the left. (The urine was still normal.)

the patients were alive five years after operation. Emmett and Kibler analyzed their cases on the basis of survival in relation to the urinary observations in

4. Medlar, M.; Spain, D. M., and Holliday, R.: Post-Mortem Compared with Clinical Diagnosis of Genito-Urinary Tuberculosis, J. Urol., to be published.

5. Wildbolz, H.: Renal Tuberculosis, J. Urol. **21**: 145-179, 1929.

6. Giles, H. H.: Tuberculosis of Kidney with Special Reference to Follow-Up Results in Squier Clinic, Surg., Gynec. & Obst. **64**: 1046-1050, 1937.

7. Emmett, J. L., and Kibler, J. M.: Renal Tuberculosis; Prognosis Following Nephrectomy Based on Preoperative Observations in "Good" Kidney, J. A. M. A. **111**:2351-2356 (Dec. 24) 1938.

8. Nesbit, R. M.; Keitzer, W. A., and Lynn, J. M.: The Prognosis of Renal Tuberculosis Treated by Nephrectomy, J. Urol. **54**: 227-234, 1945.

the "good" kidney and observed that when the urine was free from pus cells the chance for a five year cure was 43.5 per cent and the chance for a five year cure when the urine from the good kidney was free from both pus cells and tubercle bacilli was 50 per cent. The Michigan series roughly paralleled these figures, with two thirds of our cases showing five year clinical cures when the urine from the good kidney was free from pus and tubercle bacilli. These clinical results manifestly demonstrate the value of operation in treating this devastating malady, but a candid assay of the data also indicates how dismally nephrectomy has failed in nearly half the cases.

A recent reanalysis of our cases was made for the purpose of determining the factors influencing the prognosis. Complete data are available in 121 of the cases and are enumerated in the accompanying chart. These data reveal that the incidence of genital or pulmonary lesions is about the same among the patients enjoying good results as those who died or who became worse after operation, whereas the incidence of severe cystitis and the condition of the good kidney do importantly influence the prognosis. It is clearly evident that the most favorable prognosis is to be encountered in the patient who has minimal or no cystitis and whose "good" kidney is free from evidences of either obstruction or infection; but freedom from these involvements does not guarantee a favorable outcome of nephrectomy. The criterion which appears to stand out as an indication of a bad prognosis is the presence of severe cystitis. Only 4 of the patients who died had been free from this complication. Nevertheless, one third of the cured patients had had severe cystitis. It is obvious that the prognosis in any case of renal tuberculosis is hazardous and that nephrectomy is not a specific cure for the disease.

*Summary of Data on Patients Treated by Nephrectomy**

	Genital, B. & J. Lesions, Etc.		Pulmonary Lesions			Cystitis		Pyelograms (Good Kidney)		Urine in Good Kidney		
	Absent	Present	None	Minimal	Moderately or Far Advanced	None or Minimal	Severe	Normal	Hydronephrosis	Normal	Pus	Tubercle Bacilli
Cured patients	34	13	41	3	2	32	14	41	1	41	5	1
Improved but not cured	13	9	20	1	1	19	3	20	0	21	1	1
Total	47	21	61	4	3	51	17	61	1	62	6	2
Living but worse	3	1	3	1	0	3	1	1	7	0	4	1
Dead	21	28	35	9	5	4	45	9	11	29	20	17
Total	24	29	38	10	5	7	46	10	11+	29	24	18

* There were 27 deaths due to renal tuberculosis, 14 (miliary 4) to other types of tuberculosis, 6 to hydronephrosis and 2 to Addison's disease (total 49). Fifteen of the cured patients and 4 of the dead patients had only minimal or no cystitis, no genital or pulmonary disease and normal observations in pyelograms and normal urine on the side that was not diseased.

SUMMARY AND CONCLUSIONS

A reorientation of our habits of thinking in the matter of treating urinary tuberculosis is necessitated by the advent of streptomycin. Clinicians are now treating several types of urinary tuberculosis with prolonged sanatorium care and full courses of streptomycin therapy: six months should be regarded as the minimum of sanatorium care while longer periods of time are often necessary, and ninety to one hundred and twenty days of antibiotic therapy are recommended. The dosage of streptomycin is at present variable—the matter being in the investigative stage—but many have found from 1.5 to 2.0 Gm. per day to be the most effective dosage. The types of conditions that are now being treated in this manner include bilateral renal tuberculosis, residual cystitis following nephrectomy and clinically unilateral kidney lesions when there are no pyelographic evidences of the disease. At the present time most urologists are treating, by nephrectomy, the clinically unilateral lesions of the kidney that can be demonstrated by roentgenogram, and many are advocating short preoperative and postoperative courses of streptomycin to prevent the traumatic spread of the disease. When the rationale of streptomycin therapy is based on the knowledge that urinary tuberculosis is universally bilateral and that nephrectomy alone cures only about half the patients, it would seem to be illogical to withhold any therapeutic measure which might enhance the complete healing of the patient's tuberculosis. The nephrectomized patient should be afforded the same advantages of modern therapy that are considered appropriate for other patients suffering from bilateral renal tuberculosis.

Surgical removal of the grossly diseased kidney is a well accepted principle, but perhaps in the future nephrectomy can be relegated to a position below that of streptomycin and rest in the order of importance. Since it has been shown that even ulcerative renal lesions will sometimes heal during treatment with streptomycin, it would be reasonable to withhold surgical treatment, at least temporarily, in all cases of clinically unilateral renal tuberculosis. The patient should be placed on a regimen of strict rest in a sanatorium and should receive 2.0 Gm. daily of streptomycin for sixty days. At the end of this time a survey should be made to determine, by urinalyses and retrograde pyelography, the results of treatment. When the studies indicate conspicuous evidences of healing the plan of treatment should be continued for an additional sixty days, with repeated observations of the state of the lesion thereafter. The patient should then complete a minimum period of six months of sanatorium care or longer if necessary, in accordance with the needs for treatment.

If at the termination of the initial sixty day period, the patient's symptoms remain unaltered and pus and tubercle bacilli are still present in the urine obtained by ureteral catheter, nephrectomy would be indicated. Postoperatively streptomycin therapy should be continued for sixty days longer and the patient kept at rest for the prescribed six month period, or longer if need be.

Although this plan certainly will not prove efficacious in eliminating the necessity for nephrectomy in all

instances, it promises, when nephrectomy is carried out, to diminish the likelihood of miliary dissemination during operation and to militate against wound disruption following nephrectomy, and it will also serve to influence favorably the subsidence of other metastatic lesions which might still be active in the patient, particularly those in the remaining kidney, thus enhancing his chances for recovery. Our reorientation in thinking regarding the treatment of urinary tuberculosis must be predicated on a realization that operation has failed dismally in the treatment of this disease, for in the past the nephrectomized patient has had only an even chance for survival.

CONTROL OF CANCER OF THE UTERUS

Report of a Ten Year Experiment

CATHARINE MACFARLANE, M.D.
MARGARET C STURGIS, M.D.
and
FAITH S. FETTERMAN, M.D.
Philadelphia

During the ten years prior to writing, members of the Department of Gynecology of the Woman's Medical College of Pennsylvania have been conducting a clinical research on the periodic pelvic examination of presumably well women. This research was undertaken for the purpose of determining the value of such examinations in detecting cancer of the uterus, particularly the cervix, in an early and curable stage and in detecting lesions of the cervix commonly believed to predispose to cancer.

In 1938 and 1939, we succeeded in interesting the women of Philadelphia in this project. As a result, 1,319 white women, 30 to 80 years of age, presumably well, volunteered to come for pelvic examination twice a year for five years.

TABLE 1.—*Pelvic Cancers*

Location	Number of Cancers
Cervix uteri	4
Corpus uteri	2
Ovary	1
Vaginal wall	1
Total	8

Most of the volunteers appreciated the importance of the undertaking as a contribution to medical science as well as of value to themselves. With others it was a matter of passing interest. When told once or twice that they were in good condition, they grew weary of well-doing and dropped from the ranks. Some died. Some moved away. Nevertheless, we were able to make a five year report at the 1944 meeting of the American Medical Association in Philadelphia on 545 continuing volunteers.

At that time, Dr. Ludvig Hektoen, Chairman of the Committee on Clinical Research of the American Medical Association, expressed the opinion that this group of women should be followed up immediately. The examining physicians and the majority of the volunteers were eager to do this. Efforts were made to rekindle the interest of those who had dropped from the ranks. As a result, we are able to report today on 732 volunteers who have been examined more or less regularly over a ten year period.

Read before the Section on Obstetrics and Gynecology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948.

In the first examination of the 1,319 presumably well women, three squamous cell cancers of the cervix were discovered (volunteers 68, 174 and 430). Two of these were discovered on microscopic examination of areas of papillary erosion that had aroused no suspicion of malignant growth and that had been excised by the Sturmdorf technic. The third was observed on biopsy of an extensive and suspicious looking area of papillary erosion. These 3 women were treated with radium and showed no evidence of recurrence nine years after treatment.

A cancer of the uterine body was discovered on the first examination of volunteer 1140. On account of medical handicaps, treatment was limited to radium and roentgen rays. There was recurrence after nine years.

A fourth cancer of the cervix was discovered on the eleventh visit of volunteer 527. There were no symptoms, but examination revealed a smooth red polypoid growth, 1 cm. in diameter, protruding through the external os. This proved to be an adenocarcinoma.

TABLE 2.—*Social Status and Childbearing*

Category	In Original 1,319 Volunteers	In Continuing 732 Volunteers
Single nulliparous women	188	80
Married nulliparous women	224	113
Parous women	907	539

Radium needles were inserted into the growth for 1,300 mg. hours, and 2,400 mg. hours were given in the uterine cavity. Unfortunately, pyometra, general systemic infection and severe gastrointestinal symptoms developed, which made it impossible to give adequate treatment with either radium or roentgen rays. The patient died of recurrence after two years.

Adenocarcinoma of the endometrium was discovered on microscopic examination of a myomatous uterus removed supravaginally from volunteer 898 in March 1942. She showed no evidence of recurrence after six years.

A cystic tumor of the ovary was discovered on the ninth visit of volunteer 176. Operation showed this to be a rapidly growing malignant tumor, with extension to the peritoneum. This patient died of recurrence after sixteen months.

TABLE 3.—*Incidence of Cancer of the Cervix in 3,000 Gynecologic Patients*

Number of Cases	Type	Age	Cancer of Cervix
1,000	Single white nulliparous	20-77	6
1,000	Married white nulliparous	20-79	14
1,000	Married white parous	20-79	37

A cancer of the anterior vaginal wall was discovered by volunteer 1037 (a physician) just before she was due for her fifteenth visit. The growth was excised and irradiated, but the volunteer died of recurrence in the lungs after three months.

This brings up to eight the cancers of the pelvic organs discovered in our continuing group of 732 volunteers over a period of ten years. The chief interest

lies in the four cancers of the cervix. Each of these occurred in a woman who had borne a child. Four cancers of the cervix seem a small number to have developed in a group of 732 women over a period of ten years.

Our volunteers are classified according to social status and childbearing in table 2.

Deducting from the parous group 10 women whose children were born by cesarean section (whereby trauma to the cervix was eliminated), we still have 529 parous women in the continuing group.

Table 3 shows the incidence of cancer of the cervix in white women, 30 to 80 years of age, according to a previous study of admissions to the gynecologic services of the Woman's Hospital and to the Hospital of the Woman's Medical College.

While the incidence of cancer would naturally be greater in patients admitted to hospitals than in presumably well women, it is interesting to compare these figures with the observations in our research group.

TABLE 4.—*Benign Lesions of the Pelvic Organs*

Type of Lesion	Number
Inflammatory lesions of the cervix	489
Myomatous tumors of the uterus	193
Mucous polyps of the cervix	140
Cystic tumors of the ovary	40
Leukoplakic areas of the cervix	3
Papillomas of the cervix	2
Tuberculous ulcer of the vagina	1
Total	868

TABLE 5.—*Inflammatory Lesions of the Cervix*

Lesions	Number of Lesions
Endocervicitis	63
Cervicitis	53
Cervicitis with erosion	
Simple	100
Follicular	38
Papillary	105
Nonspecified	125
Total	489

On this basis, we might expect to find one cancer of the cervix in our 193 nulliparous women and twenty cancers of the cervix in our 529 parous women. So far, over a period of ten years, we have found no cancers of the cervix in our nulliparous group and only four cancers of the cervix in our parous group.

Some light is thrown on this situation when benign lesions of the pelvic organs discovered in the volunteer group are considered. In addition to the eight cancers, eight hundred and sixty-eight benign lesions of the pelvic organs were discovered in the volunteers from the begining of the research until April 1, 1948.

Most important of these benign lesions from the point of view of cancer are the 489 inflammatory lesions of the cervix. These are classified in table 5.

Some 214 of these inflammatory lesions of the cervix have been eliminated by operation, conization or cauterization. My colleagues and I believe that the development of some cancers of the cervix has been prevented by the elimination of these inflammatory lesions.

This research has cost a great deal of time, money and energy. Its results are not spectacular. Perhaps its greatest value has been educational. We must admit that in the control of cancer, education is a mighty weapon.

Our clinic is called a Cancer Research Clinic. It differs from prevention or detection clinics in that, after the original group of volunteers was recruited, no new volunteers were added. The volunteers made no financial contribution. The examining physicians gave their services without charge. The Woman's Medical College gave clinic space and nursing service.

The expense of secretarial service, of a part time medical statistician, stationery, supplies, postage, record cards, examination of pathologic specimens and other such items varied from $150 to $200 per month. This was met by grants from the American Medical Association, the International Cancer Research Foundation, the New York Medical Women's Association, the Pennsylvania Division of the Women's Field Army of the American Cancer Society and the Philadelphia Division of the American Cancer Society and gifts from private persons.

We can claim that as a result of the research three cancers of the cervix were discovered in an early stage, were treated promptly and showed no signs of recurrence after nine years; two hundred and fourteen inflammatory lesions of the cervix were discovered and eliminated, and 1,000 women and their relatives and friends have been taught the value of periodic pelvic examination.

CONCLUSIONS

Early cancer of the cervix and lesions predisposing to cancer can be detected in presumably well women by means of periodic pelvic examination. Every woman 30 years of age and over who has borne a child should be examined once a year or twice a year if inflammatory lesions of the cervix are present. Inflammatory lesions of the cervix should be eliminated.

136 South Sixteenth Street.

ABSTRACT OF DISCUSSION

DR. B. Z. CASHMAN, Pittsburgh: For more than thirty years some of us have been stressing the importance of periodic examinations for detecting cancer of the cervix, but it was Catherine Macfarlane who had the vision, industry and persuasiveness to induce 1,000 women to submit to examinations faithfully and persistently. You have heard her results. This is an excellent record and establishes the value of periodic examination in detecting cancer of the uterus in the curable stage. The low incidence of carcinoma of the cervix in her series is striking. This is suggestive that her policy of cleaning up the inflammatory lesions and the polypi of the cervix prevented cancer of the cervix. We, of the University of Pittsburgh, have been interested in the same problem but made a different approach. We have carefully examined the cervix of every woman who passed through our hands in office and hospital. If there was pronounced cervicitis present, or if symptoms of cervicitis were not relieved by conservative treatment, deep cauterization of the cervix was advised. If the patient was scheduled for surgical treatment, regardless of its nature, the opportunity was used to treat cervicitis by deep cauterization under the same anesthesia. After a series of 10,000 cases had been accumulated we attempted to determine in how many of these patients cancer of the cervix subsequently developed. Three surveys have been made. Only 3 cases of cancer of the cervix have been found in this entire group. Whether we prevented the development of carcinoma of the cervix by eliminating chronic cervicitis, as we formerly believed, or whether we destroyed cancer in its incipient stages, is of academic interest only. The important fact is that invasive cancer occurred in only a small percentage ((0.03 per cent) of this group. Until we learn more about cancer of the cervix,

the laborious methods of Dr. Macfarlane and Dr. Papanicolaou, and of our own or some similar procedure, seems to be the only true preventive measures now known. One does not need to wait for the discovery of the cause of cancer. One does not need to wait even for better methods of treatment. Doctors have now the means for eliminating cancer of the cervix if it is discovered early. It is not a problem for gynecologists alone, for gynecologists see only a small percentage of the women of this country. The opportunity lies in the hands of the general practitioners.

DR. AUGUSTA WEBSTER, Chicago: This is a unique study, one which I believe to be of great significance. These examinees were carefully screened, and no persons with symptoms were accepted for this project in clinical research. The same physicians have conducted the ten year study with 732 of the original 1,000 examinees cooperating. The continuity of the project, from the point of view of participation of both patient and physician, is a most valuable factor; too often changing personnel leads to variation in the interpretation of the same condition. The term precancerous has long been under fire, and the purists have preferred to avoid its use. The clinician, however, has always been suspicious of the relation of certain conditions to malignancy, but has lacked specific evidence to support the idea. Seven hundred and thirty-two women between the ages of 30 and 80 years were in this group who had a goodly number of minor, seemingly harmless, pelvic lesions, but in whom only eight pelvic malignant growths developed over a ten year period; four of these were cervical cancers. The four cervical malignant growths were discovered in the incipient stage, resulting in nine year cures for 3 patients. Over two hundred benign conditions were treated during the ten year period. The relatively large number of benign conditions eradicated and the small number of cancers found would certainly suggest that at least some precursors of cancer were destroyed. In apparently healthy persons many conditions may be discovered by careful physical examinations while in an asymptomatic subclinical phase. At the Cancer Prevention Center of Chicago, of 6,000 apparently healthy women, 1,015 were found to have a lacerated hypertrophied cervix, 1,288 had erosions and 223 had polyps. These figures overlap, as some women had more than one condition. In 318 instances, or 4.9 per cent, biopsy was recommended to rule out malignancy. All these persons were referred to their own family doctors for diagnostic study and treatment. It is not the intention of the Cancer Detection Clinics to alarm the examinee or to encourage other than conservative treatment of conditions found. Rather the objective is to promote effective preventive medicine and thus to insure longer life and better health to the examinees.

DR. J. HOFBAUER, Cincinnati: A rational approach in prevention of malignant conditions of the uterine cervix requires adequate knowledge of the specific etiologic and conditioning factors involved. The weight of opinion favors the view that there is an earlier predisposing phase when cellular elements that have been stimulated to proliferation present pictures of potential malignant disorder. Proliferation of polygonal cells—derivatives of the undifferentiated basal infra-epithelial cells—with the formation of one or more layers, has been observed as the cervical response to a variety of morphogenetic stimuli, notably chronic irritation, gestation and disturbed balance of the specific endocrine mechanism of the uterine cervix. It is these tissue changes with their associated deviations in functional equilibrium which have been invoked as the prologue of the cervical epithelial drama. The specific mechanism, however, accountable for the transformation of such hyperplastic preinvasive epithelium into carcinoma, is not known. The concept that cervical malignant conditions represent the sequelae of trauma incident to childbirth, cervical lacerations and erosions had remained unchallenged long enough to have become the traditionally accepted explanation. Observations made by my colleagues and me of unmistakable early cervical carcinoma in areas distinct from lacerations or erosions necessitated the search for other etiologic factors. Our experimental studies showed for the first time that the implantation into the musculature of laboratory animals of bits of fresh anterior pituitary substance evokes a rapid sequence of extensive growth phenomena of the cervical epithelium and of the uterine glands. Correlation of these observations with the recognition of occurrence of hyperplastic changes in the prepituitary as the result of repeated pregnancies created the conception of the specific hormone-induced growth phenomena in the uterine cervix—the anterior pituitary and ovarian—as predisposing factors of malignancy. Pursuit of studies concerned with the identification of inhibitors of growth responses to hormonal stimuli seems to hold the key to progress in the fascinating subject.

DR. CATHERINE MACFARLANE: Last year in this country more than 16,000 women died of cancer of the uterus. At the present time early detection is the best method available to curb the ravages of this disease. Early detection is a function of the general practitioner. In this mighty conflict he forms the first line of defense.

EMPYEMA

BRIAN BLADES, M.D.
Washington, D. C.

Empyema of the thorax has become a rare disease. This is particularly true of the postpneumococcic variety and applies to other pleural abscesses resulting from trauma and other causes. A few years ago it was a well known lesion with a significant mortality rate and troublesome morbidity and the source of controversial opinions on details of treatment. Students of medicine were warned of the frequency of complicating empyema following pneumonia, and residents dreaded the management of drainage tubes and suction apparatus. Today it is possible and probably likely that young surgeons might not have the opportunity to study an old-fashioned case of empyema of the thorax during an extended training period.

The first dramatic reduction in the incidence of postpneumococcic empyema followed the almost universal use of the sulfonamide drugs for pneumonia. For example, in 1,250 patients with pneumonia treated with the sulfonamide drugs, Dowling [1] reported an incidence of 1.9 per cent of complicating empyema. Even greater reductions in the frequency of complicating empyema following pneumonia have been reported by other authors.[2]

The almost universal use of penicillin in infections of the respiratory tract has further reduced the frequency of pleural abscesses to a figure ranging from 0 to 0.08 per cent in most series. This remarkable agent has the advantage over the sulfonamide derivatives of a strong antibacterial action when given systematically and the retention of its potency in the presence of blood and pus. Moreover, the proved low toxicity of the mold makes it possible to give enormous doses both parenterally and locally with a minimal chance of dangerous or distressing side effects. The addition of streptomycin to the antibiotic armamentarium of treatment has furnished another effectual method to combat organisms not vulnerable to penicillin.

It becomes apparent that empyema should be considered as a medical disease, with the goal of aborting frank abscesses rather than waiting for a well formed localized abscess to develop. It is important, however,

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Read before the Section on Surgery at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948.

1. Dowling, H. F.: Personal communication to the author.
2. Hurwitz, S., and Stephens, H. B.: J. Pediat. **14**: 11, 1939. Schwartz, L.; Flippin, H. F., and Turnbull, W. G.: Ann. Int. Med. **13**: 2038, 1940.

to remember that the use of these agents, which have made empyema a rare lesion, may attenuate abscess formations and change the clinical manifestations of the disease so decidedly that a diagnosis frequently cannot be made, if one thinks in terms of the type of empyema common before antibiotic therapy was available.

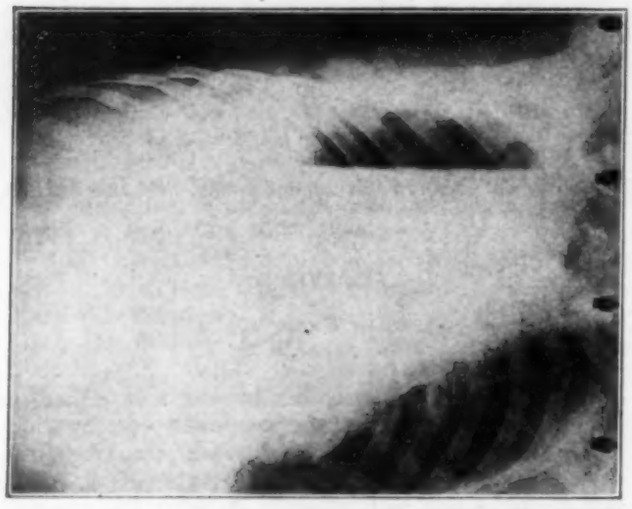

Fig. 1.—Roentgenogram taken in lateral decubitus position, demonstrating a huge empyema cavity and empyema necessitans and showing the thoracic wall at the site of empyema necessitans.

During the past war, in a study made by Blades, Hamilton and Dugan [3] of 24 cases of empyema treated with penicillin, it appeared that the early and vigorous parenteral and intrapleural use of penicillin, as soon as infected fluid appeared in the pleura, would abort the formation of frank abscess in many cases. Further experience with this type of treatment verifies the original impression. It was pointed out, however, by the same authors, that if frank thick pus forms, surgical drainage should be established and that sterile empyema is not cured empyema. Subsequent studies with both penicillin and streptomycin in the management of empyema have not altered these observations.

Proper employment of antibiotics in the treatment of empyema requires two considerations. First, the continued use of antibiotics, either locally or parenterally, without surgical intervention, after the formation of thick pus which cannot be aspirated, and therefore precludes early and complete reexpansion of the lung, should be condemned. Second, the realization that after severe pneumonia, coupled with pleural effusion, there may be some residual empyema, usually in the posterior gutter, which may escape detection for weeks or months.

An example of the misuse of penicillin in a case of traumatic empyema may be illustrated by case 1.

REPORT OF CASES

Case 1.—A young man, 23 years of age, suffered severe and multiple injuries in a serious automobile accident, including a laceration of the liver and multiple rib fractures. A hemothorax developed on the right, which received little attention, probably because of the severe abdominal injuries which required a laparotomy. Figure 1 shows the appearance of the chest eight weeks after the accident. In preceding weeks blood had been aspirated from the pleura and penicillin injected into the space. The fluid in the pleura gradually thickened and assumed the appearance of frank pus. No organisms were seen in the cultures. A week before operation thoracentesis failed to reveal pus. It is obvious that at this time the fluid was so thick that it could not be withdrawn through an ordinary needle.

A huge sterile pleural abscess developed, and after eight weeks empyema necessitans developed, pointing on the anterior thoracic wall. A thoracostomy for drainage of the empyema and incision of the thoracic wall abscess resulted in prompt healing, with no apparent permanent disability.

It is probable that early and vigorous attempts to free the pleura of fluid would have prevented the formation of the infected hemothorax and consequent empyema. The seriousness of the injury and the circumstances surrounding the accident made this somewhat difficult. Even after the hemothorax became infected, the possibility of decortication of the lung might have been considered, provided that the patient's general condition did not preclude a thoracotomy. The important lesson to be gained from this case, however, is that the use of penicillin produced a sterile abscess, but the foreign body in the pleura prevented reexpansion of the lung and healing, and, finally, by purely mechanical means sterile pus produced empyema necessitans.

This is an extreme example of the misuse of penicillin. These circumstances are more likely to occur in a case of traumatic empyema. It appears that the greatest difficulty results from the false sense of security obtained by sterilization of pus in the pleura without regard for the mechanical factors involved in the healing of an empyema cavity.

An interesting and treacherous attenuation of empyema which may follow antibiotic therapy is illustrated in case 2.

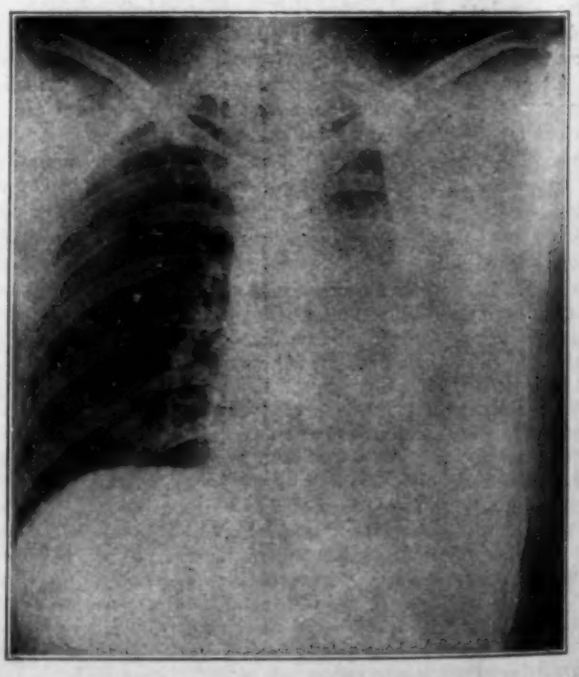

Fig. 2.—Roentgenogram revealing pleural effusion which accumulated rapidly after the onset of acute illness. The fluid was sterile.

Case 2.—A young man, 21 years of age, had a severe cold and was confined to his home for about two weeks with low grade fever, cough and expectoration. After this period he experienced a sudden chill and high temperature, ranging from 39 to 40 C. (102 to 104 F.), and massive pleural effusion developed rapidly. Penicillin was given in doses of 50,000

3. Blades, B.; Hamilton, J. E. and Dugan, D. J.: Surgery 17: 572, 1945.

units every three hours and later increased to 100,000 units every three hours. This treatment was started immediately after the chill and fever. The fluid in the chest accumulated rapidly, and thoracenteses were required every two or three days for a period of about four weeks. Cultures of the pleural fluid revealed no organisms (fig. 2). After repeated aspirations, the pleural fluid seemed to disappear and the patient's temperature fell to normal with the exception of low grade fever every two or three days. The appearance of the roentgenogram of the chest six months after the onset of illness is shown in figure 3.

Repeated examinations of sputum had revealed nothing of significance, and the tubercle bacilli had not been identified. The appearance of the roentgenogram of the chest was thought

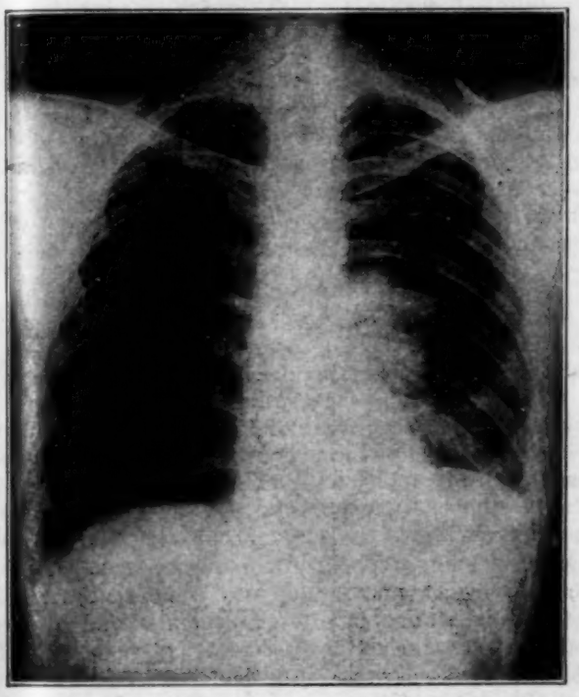

Fig. 3.—Appearance of the chest six months after the onset of acute illness. A diagnosis of tuberculosis was made based on the roentgenogram.

to indicate tuberculosis, and this patient was advised to observe strict bed rest for an indefinite period, until a positive diagnosis had been established. The patient observed strict bed rest for four months, and seven months after the onset of his illness the drainage of a small pleural abscess situated in the posterior gutter resulted in a cure. The pus contained Streptococcus hemolyticus.

This is an example of attenuation of severe streptococcic pneumonia and pleural effusion with the mistaken diagnosis of tuberculosis. Before the antibiotics were available, the erroneous diagnosis of unresolved pneumonia in cases of empyema of the thorax was common. The frequency of this mistake has been tremendously reduced, but the error still occurs. Three cases similar to case 2 have been observed, and the patients with residual empyema were thought to have unresolved pneumonia. This impression delayed necessary surgical drainage for several months.

COMMENT

In this connection it is important to remember that parenteral administration of penicillin or streptomycin may render a pleural effusion temporarily sterile. If an antibiotic is also employed locally, the possibility is even greater. After weeks or months the bacteria debilitated by the antibiotic sometimes revive enough to multiply and produce an active purulent pyogenic infection.

The obvious advantages of penicillin over the sulfonamide derivatives in the treatment of pneumonia and in cases of potentially infected traumatic hemothorax are so apparent that they require no comment. Certain principles of the use of streptomycin in the treatment of pyogenic empyema will be mentioned later.

Based on my own clinical experiences and the experimental work of Romansky, the following therapeutic approach is suggested. In cases of frank pneumonia with classic severe onset—fever, chills and other classic symptoms—penicillin should be administered immediately. A dosage of 300,000 units in one of the repository products, e. g., penicillin in wax and oil or similar preparations, is suggested. If aqueous penicillin is to be used, a dosage of 25,000 to 50,000 units every three hours is desirable. In cases with known bacteremia or in established staphylococcic infections, 300,000 units should be given two to four times daily.

If pleural fluid appears, it is important that the local treatment be withheld until an attempt has been made to identify the organisms. An initial precise bacteriologic diagnosis may rule out the possibility of a tuberculous infection or establish it and serve as a guide for subsequent antibiotic therapy. In this connection the importance of the use of penicillinase in the laboratory deserves mention. Unless the precaution is observed, the cultures may remain sterile because of the inhibitory effect of penicillin. When penicillinase is employed, this inactivation is eliminated and a positive culture may be obtained.

The dangerous toxic effects of streptomycin have already been mentioned and are well known. Reductions in dosage of this agent have greatly diminished these side actions, but they still exist and must be considered. It is important to record, therefore, that the intrapleural use of streptomycin is followed by a rapid rise in blood levels, and, if the antibiotic is to be employed locally in the pleura, reductions in parenteral dosage may be advisable until the peak of the blood level from local use has been reduced. The experimental and clinical studies of Beattie and his co-workers have established that the maximum level from intrapleural use of streptomycin is reached in from one-half to one hour after it is placed in the pleura and then falls rapidly. It is practically eliminated within four hours. This important consideration is worth recording. Since experimental and clinical evidence indicates the desirability of using the antibiotic combination, that is, combining penicillin and streptomycin, there is even more importance in precise bacteriologic diagnosis before treatment begins.

CONCLUSION

Failure to establish a definite bacteriologic diagnosis in the seriously ill patient should not be an absolute contraindication to antibiotic therapy, particularly in the case of penicillin. The significant toxic effects of streptomycin, however, make it important not to employ this agent unless there are absolute indications based on bacteriologic evidence. There are few exceptions to this principle. Relatively few organisms, which are not vulnerable to penicillin but respond to streptomycin therapy, produce pleural abscesses. The principal ones are the hemolytic influenza bacillus, Friedländer's bacillus and a few rare gram-negative bacteria.

If the intrapleural use of an antibiotic is indicated in the presence of fluid or blood in the pleura, it should be combined with systemic administration of the proper agent. If the fluid or blood continues to thicken and form frank pus, drainage or decortication plus drainage should be employed.

ABSTRACT OF DISCUSSION

Dr. Edward M. Kent, Pittsburgh: There is general agreement among surgeons in this country with everything that Dr. Blades has said concerning empyema thoracis. The two most significant observations have been that new problems have arisen in the treatment of empyema as a result of the use of antibiotics and that this complication of pneumonia resulting from the pneumococcus is seen much more rarely now than it has been in the past. It may be felt by some that it is unusual to present a paper on a problem of decreasing clinical incidence. However, I consider it highly important to do so in this instance. There are two chief reasons for this attitude: First, it is the ultimate goal of the members of the medical profession to do themselves out of a job, as it were, and strides of significant proportions have been made in that direction. However, we tend to lose sight of these accomplishments because the scope of medical practice has been extended more rapidly than it has been reduced. We are making progress in the fight to lessen or eliminate the need of surgery in the treatment of infections. Similar progress is being made in other fields of surgical endeavor excepting, of course, the repair of the results of trauma and the correction of anatomic defects. Secondly, I consider the presentation of this matter timely because, as Dr. Blades has so clearly pointed out, there are certain new problems which have been created as the result of the use of the antibiotics in the treatment of pneumonia and empyema. Dr. Blades has shown us what these new problems are, how they are anticipated and the way that he has managed them from a clinical point of view. In addition, he has sounded certain warnings which we all will do well to heed. I, for one, am in complete agreement with what he has said.

Dr. Thomas H. Burford, St. Louis: I would like to underscore what Dr. Blades has said concerning the increasing complexity with which the problem of empyema is now vested. It is true that what empyema has lost in frequency it has gained in complexity. At the Barnes Hospital, where my associates and I are now seeing approximately a twentieth of the amount of empyema that we saw in the days before sulfonamide drugs and antibiotics, we encounter problems of a vastly altered nature, and it is significant that in only a small percentage of the cases of empyema that we now see—particularly of the postpneumonitic type—is drainage done. They require a more radical type of approach. One patient whose disease was diagnosed as virus pneumonia partially recovered from the primary disease with a stiff regimen of antibiotics. A residual shadow in the posterior right side of the chest was later observed and diagnosed as carcinoma. It was not until a needle aspiration was done that it was found to be empyema. Because of the fact that the process had existed for about three months when seen, we did not drain but elected to resect the entire empyema sac. Another patient had almost certainly had typical pneumonia of pneumococcic type and had been treated intensively with penicillin. He came to us with a chest full of pus, from which nothing could be grown twelve weeks after the discovery of the empyema. Again, primary drainage was not done. A primary decortication was performed with prompt recovery. I would like to say a word about the problem of empyema in childhood. It is particularly important, now that practically all children with pneumonia are treated intensively from the very beginning with one or a combination of antibiotics, that the treatment of empyema, which may in rare cases develop, not be neglected. It is still mandatory in the very young group to institute "water-seal" intercostal drainage as soon as infected fluid is discovered.

AUREOMYCIN, A NEW ANTIBIOTIC

Results of Laboratory Studies and of Clinical Use in 100 Cases of Bacterial Infections

MAXWELL FINLAND, M.D.
HARVEY SHIELDS COLLINS, M.D.
and
TOM FITE PAINE Jr., M.D.
Boston

Unpublished data made available to us [1] suggested that the new antibiotic, aureomycin, was of low toxicity, was effective in vitro against a large variety of gram-positive and gram-negative bacteria and was particularly effective in experimental infections with rickettsias and with viruses of the psittacosis-lymphogranuloma venereum group. Clinical trials to determine its field of usefulness, therefore, seemed warranted. The results of the oral use of this antibiotic in 100 cases of a variety of bacterial infections are of sufficient interest to warrant this report. A brief résumé of the results of laboratory studies carried out in the course of this clinical study is also included. Further details will be presented in separate communications.

BACTERIOLOGIC STUDIES

Sensitivity of Bacteria.—Tests for sensitivity to aureomycin were carried out by tube dilution or streak plate methods on one hundred and eighty-six strains of pathogenic bacteria recently isolated from patients at the Boston City Hospital.[2] Strains of hemolytic streptococci, pneumococci, gonococci and meningococci were almost completely inhibited by aureomycin in concentrations of 1 microgram per cubic centimeter or less. Staphylococci and most strains of gram-negative bacilli, including typhoid and other Salmonella, were inhibited by 25 micrograms per cubic centimeter or less. Only strains of Proteus vulgaris and of pyocyaneus were moderately resistant and required from 100 to 250 micrograms per cubic centimeter for complete inhibition. There was no evidence of cross resistance with penicillin, streptomycin, polymyxin or bacitracin in any of the organisms tested. On a weight basis aureomycin was less effective than penicillin against most of the coccic organisms, but was about as effective as streptomycin against most of the gram-negative bacilli.

Stability.—Aureomycin was supplied as the hydrochloride in a dry powder in sealed ampules and in capsules. In these forms it has maintained its potency apparently unaltered for at least seven months at room temperature. It has also retained its activity for long periods in solutions that are kept frozen at —20 C. Concentrated solutions (2 mg. per cubic centimeter) in distilled water at p_H 4 retained their activity for over two weeks at 4 C. and also at 37 C. The potency of solutions in a slightly alkaline medium, in concentrations of 200 micrograms per cubic centimeter incorpo-

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This is a summary of material presented by the authors at a Conference on Aureomycin at the New York Academy of Sciences, July 21, 1948. This work was carried out with the technical assistance of Clare Wilcox, Janice M. Bryan and Paul F. Frank and was aided by a grant from the United States Public Health Service. Dr. E. Buist Wells participated in the latter part of this study.

1. The data were provided by workers of the Lederle Laboratories Division, American Cyanamid Company, who also provided generous supplies of the antibiotic.

2. The strains were isolated and identified in the Bacteriology Laboratory of the Mallory Institute of Pathology by Marion E. Lamb and A. Kathleen Daly.

rated in blood agar or 8 micrograms per cubic centimeter in saline solution, plasma or broth deteriorated rather rapidly at 37 C. and somewhat less rapidly at 4 C.

Other Factors Influencing Aureomycin Activity.—The size of the inoculum influences the concentration of aureomycin required to inhibit the growth of bacteria as tested by the tube dilution method, but has little effect, within a wide range of inoculum size, on the end points which are obtained by a surface streak method. Aureomycin is effective only against vigorously multiplying organisms, but not against fully grown or resting cultures. Aureomycin is much more effective in an acid than in an alkaline medium—the reverse of streptomycin. Attempts to demonstrate an aureomycin-inhibiting substance similar to penicillinase in filtrates of aureomycin-resistant organisms or in extracts of disrupted cells of a number of bacterial species were without success. The activity of aureomycin on cultures is not diminished by incubation in a candle jar, but higher degrees of anaerobiasis may decrease its effectiveness. Filtration of solutions of aureomycin in water, broth or urine through Seitz, Mandler or sintered glass filters does not appreciably reduce the activity of the aureomycin.

Resistance.—There was no significant tendency for the development of resistance to aureomycin in organisms either in vitro or in vivo. Of six strains of organisms repeatedly subcultured on graded concentrations of aureomycin, only one, a strain of Aerobacter aerogenes, increased in resistance thirty-two fold during thirty transfers, and no further increase in resistance occurred during forty additional transfers; the other five strains retained their original sensitivity throughout seventy subcultures. In contrast to streptomycin, resistant variants could not readily be obtained by exposure of large numbers of bacteria to high concentrations of aureomycin. All organisms of the same species isolated from the same patient before, during and after treatment with aureomycin for varying periods up to one month or longer were equally sensitive to this antibiotic.[3]

ABSORPTION AND EXCRETION

Aureomycin appears rapidly in the urine and is excreted continuously for two or three days after a single dose of 0.5 or 0.75 Gm. The highest concentrations, ranging up to 256 micrograms per cubic centimeter, are present in the urine from two to sixteen hours, and the maximum rate of excretion in the urine occurs between four and eight hours after the dose, suggesting that the optimum interval between oral doses should be about six to eight hours. Activity equivalent to between 12 and 15 per cent of a single orally administered dose can be recovered in the urine with the crude methods available.[4] Plasma levels after oral doses of up to 1 Gm. every six hours have usually been found to be about 2 micrograms per cubic centimeter or less, but the methods used were not satisfactory. Aureomycin could not be detected in bile obtained from the common bile duct during oral administration of the antibiotic, although it was not inactivated by bile in vitro.

3. Paine, T. F., Jr.; Collins, H. S., and Finland, M.: Bacteriologic Studies on Aureomycin, J. Bact. **56**: 489 (Oct.) 1948.

4. Collins, H. S.; Paine, T. F., Jr.; Wells, E. B., and Finland, M.: Urinary Excretion of Aureomycin (Preliminary Report), Proc. Soc. Exper. Biol. & Med., to be published.

CLINICAL RESULTS

The number of cases of various bacterial infections, the range of dosage used and a rough estimate of the clinical effect in 100 patients is shown in the table. Most of the patients in whom the results are listed as "doubtful" showed definite clinical and bacteriologic evidence of improvement during treatment with aureomycin, but either the results were transient or the role of the antibiotic in effecting these results could not be evaluated. The doses that were used were necessarily empiric and were increased whenever possible, in the same or in subsequent cases when the results were not optimal. No other chemotherapy or antibiotics were used during the aureomycin administration, although such agents had previously been given without success in some of the cases, particularly those with infections of the urinary tract. The results in some of the groups of cases may be summarized briefly.

Gonococcic Urethritis.—The over-all results in these cases with the doses used were satisfactory, but they were distinctly inferior to those obtained with a single injection of 300,000 units of penicillin in a prolonging agent. A number of different dosage schedules were used. Failures were most frequent among patients treated during a single day with two or three doses, or with a total of 1.5 Gm. or less. In patients receiving such doses, urethral discharge was usually still present on the day after treatment was given even when gonococci could not be demonstrated in smears or cultures at that time. Larger doses given for two days gave results approximating more closely those obtained with penicillin in the same clinic.

Summary of Results of Oral Aureomycin Therapy in 100 Patients with Bacterial Infection

Diagnosis	Number of Patients	Total Dose		Results		
		Grams	Days	Good	Doubtful	Failed
Gonorrheal urethritis, males	60*	1-3	1-2	49	11	6
Pneumococcic pneumonia	4	5-20	5-10	4	0	0
Meningococcemia, acute	1	4	3	1	0	0
Typhoid †	5	3-39	13-22	1	2	2
Salmonella enteritis, severe	2	5-7	3-8	1	0	1‡
Salmonella suppurative bacteremia (vertebral and psoas abscesses)	1	31	11	0	0	1‡
Severe infections of the urinary tract	16§	3-28	3-28	6	15	2
Escherichia coli bacteremia	1	22.5	15	0	0	1
Relapsing fever (?)	1	9-11	5-6	0	0	1
Urethritis (not gonococcic)	2	4	7	2	0	0
Typhoid carrier	1	23	31	0	0	1
Total	100	...	...	64	28	15

* Drs. Thomas F. Kaiser and Francis C. Regan and Mrs. Helen Trousdale assisted in the study of these cases.
† Four of these cases were in children; the fifth was in an adult.
‡ This patient also received 20 mg. intramuscularly every twelve hours.
§ Seven of these patients were given two separate courses of aureomycin for relapses of infection and are each listed twice under "Results."

Pneumococcic Pneumonia.—Of the 4 patients only 1 was over 60 years old and had a severe illness with jaundice, and in him treatment was started on the fourth day. The others were under 25 years old, and treatment in them was begun on the first or second day of their illness, which was mild or moderate. Each of the 4 patients had a single lobe involved, and only 1 had bacteremia before treatment was started. In each instance the temperature reached normal and the patient was clinically much improved within eighteen to thirty-six hours after the first dose of aureomycin. Pneumococci disappeared rapidly from the sputum and could not be identified by any method after the second

day of treatment. The results in these cases were comparable to those obtained with adequate doses of penicillin or sulfadiazine.

Meningococcemia.—One patient with headache, high fever and diffuse and rapidly spreading rash was treated eighteen hours after the onset of symptoms. The patient was much improved and afebrile within eighteen hours after the first dose. A blood culture, taken before the first dose, was positive for group I Meningococcus, and subsequent cultures were negative.

Typhoid Fever.—Four of the 5 cases of typhoid were in children, and in them treatment was started between the fifth and tenth day of the illness. They all had positive blood cultures before treatment, and all cultures of blood, urine and stools were negative after two or three days of aureomycin therapy. Symptomatic improvement began soon after treatment in only 1 case, but was steady and more gradual over a few days in the other 3. The fifth patient was 60 years old, and aureomycin was started in him four days after a relapse of infection with severe symptoms and bacteremia, which persisted for six days after this therapy was started. The patient then gradually improved, but his course was complicated by intestinal hemorrhage and by symptoms suggesting a perforation.

Typhoid Carrier.—One patient was known to have positive stool cultures repeatedly for at least a year before treatment was started and was the probable source of at least 2 fatal cases in a nursing home. She was given 250 mg. by mouth every eight hours for thirty-one days. During this time daily stool cultures were made, and only 1, obtained eight days after treatment was started, was positive for typhoid bacilli; the other stool cultures were all negative, but a culture of duodenal drainage material obtained on the last day of therapy was positive for typhoid bacilli. The stools again became positive two weeks after the treatment was stopped. The patient's gallbladder was subsequently removed, and its contents yielded a pure culture of typhoid bacilli. Common duct bile obtained by T tube after the operation in this case did not inhibit the action of aureomycin. Oral therapy with aureomycin was resumed after the operation, but there was no evidence of antibiotic activity in the bile during therapy with doses of 0.5 Gm. every six hours.

Salmonella Infections.—The illness in each of the 3 patients with Salmonella infections was unusually severe. The enteritis in 1 of the patients with an infection due to S. newport was improved, and in this patient the stools became formed and less frequent after aureomycin therapy, but the other patient with a similar infection with bacteremia died. The causative organism could not be recovered from the stools after treatment was started in the former, but they persisted in the latter throughout three days of treatment. In the patient with S. suipestifer bacteremia, the organisms persisted in the blood throughout eleven days of oral and intramuscular aureomycin therapy. A large intervertebral abscess and bilateral psoas abscesses were found at autopsy, and the organisms were cultured from the pus of these abscesses, from the cardiac blood and from other organs post mortem.

Colon Bacillemia.—A woman with colon bacillus bacteremia associated with jaundice, enlarged liver and an epigastric mass was improved clinically during treatment, but positive blood cultures were obtained and chills recurred after several days of aureomycin therapy. This patient died after an intestinal hemorrhage, and there was no autopsy.

Urinary Tract Infections.—The 16 patients with infection of the urinary tract who were chosen for treatment with aureomycin, with the exception of 1 with acute pyelonephritis occurring during pregnancy, all had infections of long duration, had failed to obtain any prolonged remission from many different types of therapy and had many complicating factors which militated against a favorable response. Most of them had had prolonged urinary retention, frequent instrumentation, prostatectomy, urolithiasis and recurrent acute and chronic cystitis and pyelonephritis. In the majority, the urine obtained just prior to aureomycin therapy yielded a pure culture of a single organism. Only 4 of these patients were hospitalized during the period of aureomycin therapy.[5]

In general, the pyuria in these patients diminished significantly during treatment and disappeared entirely in half of the patients while the treatment was still being given. Symptomatic relief occurred at the same time in most instances. The specimens of urine became highly acid and remained so throughout the treatment. Cultures of the urine became and remained sterile during treatment in most of the patients. In some of them, however, strains of proteus and pyocyaneus, and in 2 instances colon bacilli, either first appeared or persisted during aureomycin therapy. Infection recurred within a few days after this treatment was stopped in most of these patients, and either the same or different types of organisms were then found. The most persistent organism was Proteus vulgaris, but Pseudomonas aeruginosa also could not be eradicated. These organisms, as already noted, were the most resistant to aureomycin. Good results of a permanent nature were, therefore, infrequent in these cases of chronic infections of the urinary tract. Temporary relief, either slight or moderate, resulted in two thirds of these patients.

Nonspecific Urethritis.—Two patients were treated for urethritis which had persisted in spite of repeated treatment with penicillin, sulfonamide drugs and streptomycin. Cultures of the urethral discharge were negative for gonococci in both cases, and in 1 patient a pleuropneumonia-like organism was isolated. In the latter, a course of 9 Gm. of aureomycin by mouth over a period of six days resulted in fairly prompt symptomatic improvement with complete disappearance of urethral discharge, and subsequent cultures were negative. The other patient received 11 Gm. in five days and had rapid symptomatic improvement. His discharge had completely ceased before treatment was ended, and the infection was completely gone within eleven days.

TOXICITY

Toxic effects were minimal and infrequent. The commonest complaint during large oral doses of aureomycin was looseness of the bowels, with frequent and bulky stools, but true diarrhea was uncommon. Normal bowel action again occurred when treatment with the drug was discontinued or when the dose was temporarily decreased. Nausea and occasionally vomiting occurred after one or more doses in a few patients, but could not always be related to the treatment. An occasional patient with cystitis complained of a disagreeable sensation in the pelvis, which may have been

5. Seven of these 16 patients received two separate courses of aureomycin about two or three weeks apart.

related to the high acidity of urine during treatment with large doses. No other symptoms were noted.

Anemia attributable to the drug did not occur, and no depression in the cells in the granulocytic series was observed. There was no evidence of renal irritation as manifested by rising nonprotein nitrogen level in the blood, albuminuria or the appearance of cellular elements in the urine. There were no instances of jaundice or any other evidence of liver impairment developing after treatment was started. No fever or rashes definitely ascribable to the drug were observed. Drug fever was suspected in a child who had a recurrent elevation of temperature without symptoms after being almost afebrile after treatment for typhoid. A single dose of 200 mg. given subsequently, after the temperature had remained normal, failed to reproduce fever or symptoms, so that the relation of the drug to the recurrent fever could not be evaluated.

CONCLUSIONS

These observations suggest that aureomycin has definite antibacterial activity against many micro-organisms, including coccic and bacillary forms, and it may prove useful in the treatment of infections with organisms that are resistant to penicillin or to streptomycin.

Aureomycin given by mouth, in the doses used, appeared to have a definite beneficial effect in coccic infections. The results in cases of gonorrhea were inferior to those obtained with adequate doses of penicillin. The results in some of the patients with typhoid and Salmonella infections appeared to be favorable, but in most of the cases the effects were equivocal. In the infections of the urinary tract, considering the types of cases treated, the results were favorable and were probably comparable, if not superior, to those obtained with the use of streptomycin or sulfonamide drugs in similar cases. Infections with Proteus vulgaris and Pseudomonas aeruginosa, however, were not much benefited by aureomycin. The only evidence of toxicity was the occurrence of loose bowel movements when large doses were given by mouth. Resistant organisms did not develop during treatment with aureomycin, and resistant variants could not readily be produced in vitro.

While the observations of other workers, both in experimental animals and in human beings, suggest that the major field of usefulness of aureomycin may be in the treatment of infections with rickettsias or with viruses of the psittacosis-lymphogranuloma venereum group, the results in the present cases suggest that aureomycin may be useful in a large variety of bacterial infections. It therefore deserves a more extended clinical trial.

Hemometakinesia.—The concept of hemodynamics, to which the term hemometakinesia has been applied, provides, it is believed, a more rational approach to the management of certain forms of peripheral vascular disease than now exists. This concept is based on certain observations concerning the physiology of the circulation which established the presence of spontaneous and even rhythmic fluctuations in the volume of organs, primarily attributable changes in the volume of the blood within the part. These observations, which suggest that there is a continuous shifting back and forth of blood from one part of the body to another, seem to indicate the existence of a well regulated "borrowing-lending" mechanism which permits the body to utilize its limited blood volume in the most effective manner to meet variations in local requirements.—DeBakey, Michael E.; Burch, George E., and Ray, Thorpe, *The Journal of the Michigan State Medical Society*, June 1948.

TREATMENT IN A PSYCHOSOMATIC CLINIC

Preliminary Report

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The treatment of the great number of patients with bodily disturbances and with emotional reactions occurring as part of the human organism's response to adverse life situations is an urgent medical problem. The present report is based on experiences in treatment with 889 such patients seen in a newly organized medical outpatient clinic over a period of two years. Six hundred and ninety of them were followed up for more than a year.

METHOD

The patients ranged in age between 5 and 69 years. Sixty per cent were female, and 40 per cent were male. They suffered chiefly from bronchial asthma, hypertension, vasomotor rhinitis, migraine, urticaria, hypoglycemia, dermatitis, peptic ulcer, mucous colitis, ulcerative colitis and phenomena of muscle tension.

In addition to the usual medical history and examination with appropriate laboratory tests, a personality study was done. Special note was made of the family and cultural background. The state of the patient's health was correlated with events, overt activities, attitudes and emotional responses. The objective was to understand the motivations and mechanisms of disturbed function. Treatment was aimed at altering the disordered pattern, so that the patient might achieve more adequate utilization of his capacities toward a greater satisfaction and a more salutary integration. Insofar as was possible, physiologic changes, qualitative and quantitative, were correlated with the emotional reactions and behavior pattern of the patient under varying life situations. Then an attempt was usually made to explain to the patient what had been happening to him, in order that perplexity might be replaced by a grasp of the dynamic mechanisms at work. The past experiences and reactions were integrated with the present in order to increase insight into his life adaptation.

RESULTS

Of the 690 patients, 113 were considered by their physicians to be symptomatically and basically improved. Two hundred and thirty-four were considered only symptomatically improved and 343 unimproved. One hundred and ninety-one of the 343 patients in the unimproved category attended the clinic for less than a month, and of these 82 received no treatment. If those who received no treatment were excluded, 19 per cent were basically improved, 38 per cent were symptomatically improved and 43 per cent were unimproved.

Thirty-one per cent discontinued coming to the clinic without any explanation. Follow-up studies revealed that about 60 per cent of these felt that they had improved. They were not, however, included in either of the aforementioned improved categories.

The designation symptomatic improvement was applied to those patients who had shown a definite and

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Aided by grants from the Commonwealth Fund and the Lester N. Hofheimer Foundation.

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Read before the Section on Nervous and Mental Diseases at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 23, 1948.

sustained diminution in signs and symptoms over a period of at least a year. Basic improvement depended on the symptomatically improved persons having encountered a major threat in their life situation and having shown a reorientation in outlook by meeting it in a more constructive way and without symptoms.

EVALUATION OF VARIOUS THERAPEUTIC PROCEDURES

No absolute distinctions between therapeutic procedures could be made, and no one method could be administered in pure culture. Nevertheless, each physician delineated as far as was possible the treatments used and the value of each. The chief procedures and the number of cases in which they were used successfully were as follows:

Reassurance and emotional support	309
Free expression of conflicts and feelings	304
Advice regarding attitudes, habits and activities	173
Explanation of psychophysiologic processes	130
Symptomatic drug therapy	123
Intravenous use of "sodium amytal" (sodium isoamylethylbarbiturate)	112
Ruling out neoplastic and infectious disease	112
Dealing with other members of the family	101
Development of insight	99
Analysis of emotional development	81
Attempts to modify situation	71
Dream analysis	52
Help from Social Service Department	30

Reassurance and emotional support employed the human warmth of the physician and was helpful in enhancing the strength, faith and determination of the patients as well as in releasing inhibitions and repressions. It implied an understanding and tolerant attitude on the part of the physician and included recognition and praise for the assets and achievements of the patient. It also involved an unswerving interest in and concern for whatever problem or question the patient brought to the doctor. In short, without becoming too identified with the patient's problems the physician attempted to play the role of a strong authoritative, but not authoritarian, thoroughly dependable friend of the patient.

Free expression of conflicts and feelings through verbalization promoted a release of tension and often resulted in relief from anxiety and resentment and less need to act out emotional conflicts in a socially undesirable manner. Patients repeatedly stated that the free expression of their conflicts had given them a sense of relief and had aided in an understanding that was of the greatest help to them. Many complained of previously not having been permitted to talk, of having been told that there was nothing wrong, that they imagined they were ill or that they should forget their symptoms.

There appeared to be no short cut for allowing the patient to find out about himself by discussing himself frankly with a tolerant physician. When direct questions were asked bluntly the patient often felt that he was being cross examined, and an attitude of antagonism resulted. When he was allowed to talk at his own pace, however, relevant conflicts and significantly traumatic situations were relatively easily brought out.

The patients were encouraged to discuss the advantages and disadvantages of a given situation before making important decisions. Helping them to take independent action led to the development of a greater feeling of security and capacity to deal with ensuing problems. However, at certain times, when the psychodynamics had been clarified, direct practical advice was helpful in enabling them to break away from unhealthy fixed habit patterns. Such advice, coming from a physician, relieved the patient of responsibility and guilt, so that he could make constructive decisions which might otherwise have been delayed indefinitely.

An analysis of the emotional development during infancy, childhood and adult life was elicited by a biographic review and also by allowing the patient to associate freely about significant life events and his reactions to them. Recall and interpretation of dreams through spontaneous association by the patient facilitated the uncovering of emotional conflicts. The feeling of security engendered and the release of emotional repression aided in establishing healthier patterns of bodily function and in the development of more mature attitudes and behavior.

Intravenously administered "sodium amytal" was of value in the alleviation of troublesome symptoms, in the elucidation of dynamic mechanisms and in gaining therapeutic leverage.[1]

Frequently considerable improvement was achieved without the verbal expression of insight. Many patients who appeared to have developed some comprehension of the dynamics of their illnesses expressed it rarely or not at all. In some of these pride and a need for a feeling of self sufficiency interdicted an admission of improved integration. However, it was often conveyed indirectly to the physician.

The recording and measurement of physiologic disturbances and correlating them with the emotional reactions and behavior of the patient in varying life situations served to promote an understanding of the total biologic response and was often followed by improvement. This method was especially helpful to patients who came to the clinic perplexed about the nature of their disorder or apprehensive of its being a serious or perhaps fatal disease.

Interviews with other members of the family led to improvement in interpersonal relationships and decrease in anxieties and resentments in the home. These were usually carried out by the physician, but sometimes by the social service worker. The Social Service Department was also helpful in obtaining employment, arranging for convalescent care, making plans for children of patients and carrying out follow-up studies.

Drugs were used to afford symptomatic relief. They were usually employed to tide the patient over a difficult period in his illness, and their use was discontinued as soon as possible.

FORMULATION

It has been possible satisfactorily to treat in a medical outpatient department patients with various psychosomatic disorders and effect fundamental and lasting improvement in 1 out of 5 and at least symptomatic improvement in more than half of the group treated.

The bodily disorders and diseases were viewed as biologic reactions of defense against threats arising out of problems of interpersonal and situational adjustment.

The clinical course also gave support to the concept that the patient, in an effort to deal with adversity, invoked faulty emergency measures[2] which often led

1. Horsley, J. S.: Narcoanalysis, New York, Oxford University Press, 1943. Grinker, R. R., and Spiegel, J. P.: War Neuroses in North Africa: The Tunisian Campaign (Jan.-May 1943), New York, Josiah Macy Jr., Foundation, 1943. Ripley, H. S., and Wolf, S.: The Intravenous Use of Sodium Amytal in Psychosomatic Disorders, Psychosom. Med. 9: 260-268 (July-Aug.) 1947.

2. Rado, S.: Developments in the Psychoanalytic Conception and Treatment of the Neuroses, Psycho. Analyt. Quart. 8: 427-437 (Oct.) 1939.

to illness and to tissue damage. The aim of the reaction patterns was often at variance with the conscious purposes of the patient,[3] and this accentuated the conflict.

A variety of types of relationship between patient and physician was found useful, as was flexibility with regard to the number and frequency of visits.

The depth of treatment attained depended on the ability of the patient to use his resources in developing improved patterns of reaction, rather than on the frequency of the interviews or the duration of the treatment. Diethelm[4] recognized the importance of flexibility in carrying out a plan of treatment. This was later emphasized by Alexander and French.[5]

An average of only nine hours per patient was spent, and no patient received more than eighty-five hours of clinic time during the two years of follow-up. At the end of the period of evaluation many of the patients were still being seen at intervals, but usually not more often than once a month.

The following assets presaged improvement:

1. Recognition of failure of present patterns of adjustment and desire for help
2. Confidence in and ability to cooperate with physician
3. Flexibility of personality structure
4. Disorder of recent origin
5. Capacity and willingness to assume responsibility in treatment
6. Past record of constructive interpersonal relationships
7. Past record of ability to derive satisfaction from occupation, religion, sports, lodges and other activities
8. Willingness of family to cooperate

The opposite characteristics were found among those for whom treatment was not successful. When a patient had not at least some of these assets, and if he had not shown some improvement after two months of this treatment, it was unlikely that he would benefit appreciably from a more prolonged period of treatment. There is not evidence enough as yet, however, to be sure of such a categoric generalization.

The most powerful therapeutic force stemmed from the ability of the physician and the clinic to inculcate in the patient faith in himself and the capacity to recognize and deal constructively with his problems. This usually involved a reorientation of attitude and entailed far more than a personal attachment to the physician. Only when he had acquired such faith and confidence was it possible for him to abandon costly inappropriate emergency patterns and deal more directly and constructively with threats and challenges of day to day living.

ABSTRACT OF DISCUSSION

DR. HENRY W. BROSIN, Chicago: I think that the report by Dr. Ripley and Dr. Wolf of 19 per cent basic improvement and 38 per cent symptomatic improvement would agree with the incidence observed in many other clinics; that is a respectable showing. I have every sympathy with their definitive phrasing in itemizing the thirteen methods used and the eight prognostic factors, but hope that in future studies the factors on which these various methods and prognostic criteria are based will be more clearly described. That is the heart of the problem in studying prognosis. This is an excellent study, but we need more definitive work in order to make it useful to the day to day practitioner. Flexibility in treatment is highly desirable, but the more precise definition of the methods used in terms of a specific patient-physician relationship is incumbent on the authors. There is no question in my mind that Dr. Ripley and his skilful associate have a systematic goal, but the actual details need fuller description. The authors point out that the necessity of learning the action patterns and the dynamics rather than the mere description of the patient's difficulties; I would add that we need more familiarity with these patterns. We need to be comfortable with the patient; otherwise, second rate settlements are made, even though these may result in favorable symptomatic improvement. I would like to call attention to the studies of Dr. Thomas French, who pointed out that perhaps one of the best methods of studying the efficacy of individual therapeutic technics—the actual relation between patient and physician—may be studied through the means of the individual unit of work done; a specific problem of the total constellation is carried from the beginning to a point of progress. A series of such units may give much better insight as to the methods, mechanics and basic improvements than a casual, a more superficial, total evaluation. The importance of sound recording for the future of prognostic studies, I think, cannot be overestimated.

DR. ROY R. GRINKER, Chicago: When one talks about psychotherapy it is necessary to understand exactly what one means. One can no longer equate it with some sort of refined common sense approach to a patient's problems, because it now includes procedures which have been highly developed and refined for specific disturbances and it consists of many highly specialized technics. In research in the field of psychotherapy there is no longer concern with statistical reports which state that so many patients were improved, cured or unimproved. These categories even with numbers give little information regarding the real problems of psychotherapy. It can be stated in general that interest lies in knowing what kinds of physicians treat what sorts of disturbances with what specific technics and get what results. By "disturbance" one does not mean a heading or a label in a diagnostic classification, but a specific dynamic formulation obtained from a detailed understanding of the patient's inner and external problems, his vulnerability to failure or success in special life situations with those problems and the methods with which he handles them. The methods with which one treats these disturbances must no longer be classified simply as psychotherapeutic. They must be classified scientifically in detail in terms of the exact procedures of intervention and their specific indications. Helping patients through social service, as one author stated, is not understandable as a system of treating patients. To say that there are thirteen methods which are all used at one time or another in the treatment of a single patient is interesting, but when is one method used? In what dynamic state does one use that one method to solve what problem, and with what results? Millions of dollars are being spent in psychiatric clinics, in psychosomatic clinics, and hundreds of persons are spending a great deal of time in applying therapeutic technics, and yet there is no awareness of the efficacy of any of these therapeutic ventures except in such general terms as have been stated in this paper. It is time to come to terms with specificity in relation to exactly defined entities of psychologic disturbances, in order that this may result in a specialized knowledge that may be retransmitted to the practitioner as "common sense."

DR. H. S. RIPLEY, New York: Perhaps we have covered too large a group of patients and too great a variety of clinical problems to give significant details about individual treatment; however, we have felt that it is important to try to delineate methods of treatment and make some approximation of their value. Our report is based on experience in the Psychosomatic Clinic at the New York Hospital, where the eleven physicians who were carrying out the treatment met in conferences to define the methods we have listed and evaluate their use. The result is a composite picture of their experiences. We need to continue to try to investigate carefully the questions raised by Dr. Brosin and Dr. Grinker. More specific indications for the various categories of treatment should be worked out by those studying psychosomatic problems; however, the complexity of the clinical syndromes and the variability in the personalities of the patients and the therapeutists make it necessary frequently to alter plans of treatment. The need for flexibility has to be kept in mind constantly.

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3. Wolff, H. G.: Protective Reaction Patterns and Disease, Ann. Int. Med. **27**: 944-969 (Dec.) 1947.
4. Diethelm, O.: Treatment in Psychiatry, New York, The Macmillan Company, 1936.
5. Alexander, F., and French, T. M.: Psychoanalytic Therapy, New York, The Ronald Press Company, 1946.

VERIFIED REFRACTION

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This paper describes a refraction routine in which throughout the examination one method of testing is used to check or verify another. In this way most of the common blunders are detected. This practice is particularly valuable for students and for general practitioners who perform a limited amount of refraction. It also has merit for experienced examiners.

At the Board examinations even the well prepared candidates usually show familiarity with only one way of refracting. The method chosen varies, but they use some one technic exclusively. Many of them can describe the theory of other common methods, but have never tried them. Others who have tried them never developed any facility with them. They reverted to their original technic, not because it was best, but because it was familiar.

At first thought this may seem rather commendable than otherwise. We are somewhat conditioned to the idea that if a refractionist can get results by any means, that is as much as can be expected of him. Why then should he not perfect himself in his one system and stick to it? There are several reasons. The first is somewhat theoretical. Surely with their pretensions to superior knowledge, ophthalmologists ought to be more widely informed. A more practical reason is the universal experience that every method, no matter how perfect in theory, fails occasionally. None is infallible. All of them are subject to error, but as they are based on different principles the same mistake does not occur with all. One method will check the accuracy of the others and will supplement them. This ought to be reason enough for all popular methods to be taught to all students. Another reason is that no refractionist is fitted to compare results of different technics until he can perform them dextrously. He does not know which is best.

In over half of all cases all methods of refraction, dials, cross cylinders, cycloplegia and fogging have almost identical results in the hands of experts. It is the other type of case, in which tests disagree, that causes trouble. This is the reason for outlining a refraction routine here which compares the results of different methods and yet is fast because it involves few changes of lenses. It is a good routine for teaching. It is also practical for office use. It is thorough and does not leave undone some test which may later reveal a mistake in the prescription and discredit the examiner.

Records properly begin with the history and visual acuity. The history will reveal certain symptoms which characterize certain anomalies of refraction. The complaints of presbyopic persons constitute an outstanding example. The data on visual acuity will show that different degrees of impairment of distant vision are consistent with different refractive errors, as for instance myopia.

Use of the pinhole is apt to give a rough idea of the possibility of correction.

With this information begins the streamlining of this routine. Preliminary noncycloplegic retinoscopy is the most revealing single test. This gives a preview of the patient's prescription. It is like getting the answer out of the back of the book. It does away with the fumbling called trial and error—mostly error—involved in so-called manifest refraction. Without it several changes of trial frame lenses have to be made before the examiner has any idea whether he is dealing with a hyperope or a myope. In the presence of much astigmatism, he is not even sure of this. I have seen a candidate for the Board take twenty minutes to get information that would have been revealed by a single flash with the retinoscope and then get it wrong. Even if the doctor does not value his time he introduces a source of error every time he wears down his patient. Patients should be relaxed and leisurely.

With the newer self-illuminating retinoscopes, observation through a closed pupil is an easy trick. Fortunately, young persons, whose accommodation is most troublesome, usually have large pupils. The results are by no means to be accepted as absolute, yet in about three quarters of the cases they are fairly reliable, and surprisingly often they give the exact sphere and cylinder of the final prescription.

Since speed is an object, an apparatus is helpful, permitting rapid changes of lenses, like a phoroptometer or Green's refractor. Dry retinoscopy may be accomplished in two ways. One is with the patient looking at distance; the other is with the patient looking at the retinoscope. One method may be used to corroborate the other.

NONCYCLOPLEGIC EXAMINATION

No excuse is needed for the teaching of expert noncycloplegic refraction. Not only is it in skilled hands often more potent than cycloplegia but it also is the best check on the action of cycloplegic drugs, which are sadly erratic. It is the only recourse when mydriasis is contraindicated. Many candidates suffer from the delusion that when cycloplegia fails, nothing else can work. Most of them never have learned how to perform competent "dry" refraction.

ASTIGMATIC DIALS

Leaving in the trial frame, unchanged, the highest plus sphere (or lowest minus sphere) found by dry retinoscopy should automatically provide the fogging sphere required for use with the astigmatic dials. This then is the moment to use this test. The common cause of failure with dials is inadequate fogging. Overfogging is also misleading. As retinoscopy is not entirely trustworthy, in order to determine whether the posterior plane of the conoid is exactly on the retina, a plus sphere may be added, which should increase the blur. The favored method is to expose the clock dial or sunburst of the Lancaster-Regan or the Verhoeff charts. With proper fogging, the most distinct line lies in the axis of the plus cylinder. Replacing the clock with the cross dial, the examiner places one cross line on this axis. Transverse to this is the blurred minus axis. This axis is cleared by concave cylinders, increased until the two crossed lines exactly balance.

There should now be some family resemblance between the result of the dial test and the result of dry retinoscopy. The retinoscopy is so temperamental that a surer check of the dial test is needed. Lancaster,[1] in his original paper in 1915, recommended confirming the axis by rotating the cylinder. This is an early instance of verified refraction. The power may then be tested by alternating equal cylinders before the trial case correction at opposite axes.

Read before the Section on Ophthalmology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948.

1. Lancaster, W. B.: Subjective Tests for Astigmatism, Tr. Am. Acad. Ophth., 1915, p. 167.

CROSSED CYLINDERS

Now is a favorable time for the use of cross cylinders as a further check on astigmatism. With the same correction in the trial frame, the examiner tests the axis by flipping the cross cylinder with the handle held in the axis thus found. He then holds the axis of the cross cylinder in this axis and flips again. This tests the power.[2] A modification of the cross cylinder test is the "subtraction test" [3] I described years ago. If any two of these tests agree, the chances favor the result so obtained. The one giving the best visual acuity is usually the correction of choice.

SPHERICAL ERROR

The tests for astigmatism can be performed with only an approximate knowledge of the sphere, but the sphere cannot be determined accurately without the correct cylinder. This routine is now at the point where the cylinder has been determined and is set up in the trial frame. Nothing further is therefore needed to proceed with the fogging test. At present the approved method is to add plus spheres, making the eye artificially myopic. The blur resulting is then reduced by diminishing the plus overcorrection step by step. In response to increased blur by ciliary action, the eye is supposed to relax. Usually that is what happens, though not invariably. Usually greater relaxation takes place if both eyes are seeing and are unfogged simultaneously than when each eye is unfogged with the other covered. This often amounts to as much as 0.75 D. About twenty years ago Burdon-Cooper [4] reported to the English Speaking Congress on a series of cases in which binocular fogging was more potent than atropine. Shortly after this Dorland Smith [5] introduced what he called "cyclodamia." This is a binocular technic. It unfogs from complete blur. This is produced by adding more than + 1.50 to the spheres found by dry retinoscopy combined with the cylinders last determined. The method is distinguished by noting three levels of blur. The levels to be watched for: (1) when binocular vision is 6/60 (20/200)—the eyes are fogged by about + 1.50; (2) when the 6/12 (20/40) line is visible—the fogging is about + 0.50, and (3) when this + 0.50 is removed, the 6/6 (20/20) line should be read. This is not usually the lens affording clearest sight, but is a slightly higher correction. The fog is then almost lifted. This is the time to equalize the correction of the eyes. Usually the vision is equal when the fogging sphere over each eye is the same. If the sight in one eye is not as good as in the other, that eye is probably more heavily fogged. It should be unfogged until the vision is equal in both eyes. Therefore, as 6/6 (20/20) is seldom the patient's best acuity, vision is usually still slightly overcorrected on the plus side, so that the eyes are cleared a little at a time until the best vision is obtained. While Smith's levels are not as exact as this rule implies, they are about as reliable as any refraction tests.

NEAR POINT TEST

Both eyes at this point should have the same near point. This near point should also correspond to the age of the patient. The test is made without alteration of the lenses in the trial frame except that in presbyopia addition of a sphere is required to permit reading. These spheres should be equal in the two eyes and correspond to the age.

There are now three checks on the sphere: (1) the dry retinoscopy, (2) the cyclodamic levels and (3) the near point test. The different observations which should tally, if the examination so far is trustworthy, are:

1. The complaint and history
2. The visual acuity (including pinhole)
3. Preliminary retinoscopy (with variants)
4. Astigmatic dials
5. Cross cylinder test
6. Cyclodamia (three levels)
7. Near point test

If the sequence outlined is followed, it will be seen that the changes in lenses in the frame are reduced to the minimum.

1. The final sphere of the retinoscopy is also that used for the dial test.
2. The lenses left by the dial test are used unchanged for the cross cylinders.
3. The cylinders which result from the tests for astigmatism are not touched again, but carry through the fogging test.
4. For cyclodamia both sphere sides of the phoroptometer are rotated equally and reduced simultaneously. Notation is made of the three levels.
5. The acuity is then equalized.
6. The unfogging is completed.
7 The lenses so found are those used for the near point test.

The advantage of this method of simultaneous binocular fogging should be obvious. It is often three quarters of a diopter more effective than uniocular fogging, and it is the only method, either dry or cycloplegic, in which it is possible to handle both eyes at the same time, eliminating one test.

CYCLOPLEGIA

It is preferable to make routine use of cycloplegia in young persons with active accommodation. To be sure, a few oculists take the position that in the hands of seasoned examiners nothing can be accomplished with cycloplegics which cannot be as well or better effected without them. Even they are rather tolerant of the recommendation that novices should examine with cycloplegics. A recent study [6] found 16 per cent of patients showing 0.75 to 1.00 D. more hyperopia or less myopia with cycloplegia. This means that cycloplegic examination is sometimes more effective, just as at other times dry refraction gives more complete relaxation. Neither is as uniformly reliable as advocates like to believe.

Cycloplegics also tend to allay the tension engendered by emotional stress. This property is as useful as the effect on the accommodation, which is rather fallible. Unless contraindicated, as by a shallow anterior chamber, cycloplegia should be used on the chance that something of importance may be revealed. It is useful if only to confirm the noncycloplegic observation, when dry tests give inconsistent results.

Under cycloplegia, to avoid the customary "static refraction" with hit or miss changes of sphere, and if necessary also of cylinder, aimed at giving 6/6 (20/20) acuity, the routine followed is theoretically similar to that just outlined for dry refraction, cylinder first and then sphere, with best vision the criterion: (1) retinoscopy, (2) cycloplegic acceptance of cylinder with dial tests and cross cylinders, (3) choice of sphere at trial case and (4) near point test for residual accommodation.

2. Crisp, W. H.: A Plea for Use of Cross Cylinder, Tr. Am. Acad. Ophth., 1922, p. 178.
3. Beach, S. J.: Correction of Low Astigmia, Tr. Am. Ophth. Soc. 40: 63, 1942.
4. Burdon-Cooper, J.: The Behavior of the Crystalline Lens System in Artificial Cycloplegia, Tr. Ophth. Soc. U. Kingdom 45: 386, 1925.
5. Smith, D.: Refraction Under Cyclodamia, Am. J. Ophth. 9: 896, 1926.
6. Bannon, R. E.: Use of Cycloplegics in Refraction, Quart. Rev. Ophth. 4: 144 (June) 1948.

These tests should confirm the precycloplegic tests. They should also be consistent with one another. If the cycloplegic tests for sphere and cylinder confirm the dry refraction, then the duplication is usually unnecessary.

Usually the cycloplegic tests will confirm the precycloplegic observations. Results can then be accepted for prescription of lenses. Because these methods of examination so often produce identical results, most ophthalmologists tend to omit one or the other and thereby lose the chance to check their results.

POSTCYCLOPLEGIC EXAMINATION

The use of cycloplegics may uncover some blunders in the dry tests. When they differ from the precycloplegic observations, a postcycloplegic examination is necessary. The cycloplegic tests alone cannot be relied on for two reasons. The dilated pupil exaggerates the aberrations of the eye. The cycloplegia is itself uncertain. Vision with the dilated pupil may not be quite as accurate. The postcycloplegic tests follow the precycloplegic routine. Contrary to custom, it is often advantageous to make the postcycloplegic examination before the cycloplegia is entirely worn off, so that asthenopic influences are in abeyance.

SUMMARY AND CONCLUSION

This paper is inspired by the limited knowledge of refraction exhibited by candidates for the Board examination. Even the candidates who obtain satisfactory results at the practical examinations show training confined to only one of the standard methods. Young assistants can usually operate on cataracts better than they can fit patients with glasses.

The paper presents a sequence which permits all tests to be checked by other technics, based on different principles. By following the order indicated few changes of lenses are needed, so that the routine is fast as well as accurate. It is useful for teaching and for occasional fitting of glasses by general practitioners. It is also well adapted to routine office refraction.

For clearness the details of the tests available in treatises on refraction have been omitted. So, also, are variants, such as choice of cycloplegics, refraction with plus cylinders instead of minus and cylinder retinoscopy, which do not materially affect the use of the routine described. In general, ophthalmologists use some approved method of refraction and trust to luck that it will give correct results. The results should be verified to enable one to be as certain as possible.

ABSTRACT OF DISCUSSION

Dr. M. Hayward Post Jr., St. Louis: Today the problem of the relation of the medical profession to the art of refraction is one that is uppermost in the minds of all thinking ophthalmologists. It is only through complete understanding of the physiologic and pathologic processes of the complex organ of sight, and its close relationship to the body as a whole, that this examination can be properly carried out. It is only through our ability to give the highest grade of service, thereby achieving the finest results, that we may hope to retain the confidence of the public. Dr. Beach has pointed out the simple obvious facts, but I regret to say that the lesson to be learned therefrom, in my experience in conducting the examination of students of all ages, has, as a rule, not been put into practice. This is all too often true, not only of the young and inexperienced, but even more so of the older and busier practitioner. The fundamental difficulty lies in the graduate training in the eye departments of the medical schools. Here great stress is laid, as it should be, on retinoscopy under a cycloplegic. The mentality, and frequently a language difficulty, often make this type of examination a necessity in clinical work. But in private practice, where the grade of intelligence is higher, and the time of the average patient more valuable, such a procedure in all cases is neither practicable nor desirable. Here the art of "dry refraction" becomes of vastly greater importance, and many young ophthalmologists, fresh from clinical training, are at a loss as to the proper procedures. One aspect of this tendency toward onesidedness may be gleaned from the setup in many of the largest clinics, where the use of the astigmatic dial is, apparently, a lost art. This is harmful. At least as a check-up on other methods of refraction it is of the greatest value, and, indeed, in the hands of experts gives a rapid and exact method of estimating astigmatism, especially when combined with the use of the crossed cylinder. The older ophthalmologist often falls into a rut and, from lack of time and greater interest in the more spectacular aspects of surgery and pathology, fails to "verify" his refraction. The result is that the majority of older ophthalmologists are notably poor refractionists. The teaching of refraction should not be left solely in the hands of the residents and younger members of the staff, but it should be carefully and conscientiously supervised and controlled by the more experienced of the faculty.

Dr. Hugo L. Bair, Rochester, Minn.: Refraction has two correlated aspects: one is the precise optical examination of the eyes and the other is to provide comfortable vision which is satisfactory for the patient's requirements. Dr. Beach's excellent paper stresses the first aspect. He includes the history as a part of the procedure. This is extremely important with regard to the second aspect of the refraction. The examiner should decide, if possible, whether or not the chief complaint is likely to be related to use of the eyes and whether or not any refractive error or imbalance of the ocular muscles could be the basis for it. This decision is significant in the determination of the final prescription. It is also important to know what vocational and avocational demands are made on the patient's eyes. Dr. Beach mentions retinoscopy as the preliminary step in determination of the refractive error. Too often, in the teaching of refraction, either insufficient emphasis or wrong emphasis has been placed on retinoscopy. It can be more than simply a rough guide to the degree and type of refractive error. In Dr. Beach's system of refraction retinoscopy assumes a place along with other procedures. The findings on retinoscopy should be checked by, and should also be a check on, the procedures. It is as valuable in cyclodynamic as in cycloplegic refraction. In case of a normal pupil and no cycloplegia, retinoscopy should be done by fogging; the more hypermetropic meridian should be slightly overcorrected on the plus side with a sphere. The sphere is left in place in the trial frame and a minus cylinder then is used to determine the astigmatism. If the combination thus found is left in place, it can be used as an immediate basis for the subjective refraction. An important principle that is not sufficiently emphasized in the teaching of refraction is the production of rapid contrasts to determine the best correction. Use of the cross cylinder brings this out very well in the determination of astigmatism, but the same principle is applicable to the determination of the spherical correction for the single eye as well as in the comparison of the corrections in the two eyes. In determination of the spherical correction for the single eye, a small plus and an equally small minus sphere are quickly interchanged in front of the eye and the correction in the trial frame is varied until the same degree of blur is produced with each of the check lenses. Rapid interchange does not allow time for the small minus sphere to be overcome by accommodation.

Dr. Joseph I. Pascal, New York: Dr. Beach mentioned the use of the cross cylinder in connection with the line charts. It cannot be emphasized too strongly that these two methods of examination differ radically in the method of application. It has been shown, and can be shown by the study of the retinal images and also mathematically, that a cross cylinder works best only when the eye is not fogged, that is, when the eye is in a condition which may be called meridional balance. In this

condition the astigmatism has been changed to mixed astigmatism, whereas the line charts work best only when the eye is fogged, slightly fogged or half fogged. With reference to refraction in general, Dr. Beach has well shown that there is need of having more than one method at one's command, but there is one point in this connection which needs to be mentioned, that is, different methods of examination will frequently give slightly different results, occasionally decidedly different results. The most plausible explanation for this observation is that the different zones in the pupil generally have somewhat different refractive errors; for example, with a 4 to 5 mm. pupil, if one isolates a 2 mm. zone in the lower part of the pupil, one often finds a different refractive condition from what one would find in a 2 mm. zone situated at some other part of the pupil. When one examines the eye with the pupil exposed as a whole, the result is really an average of different refractive conditions of the different pupillary zones. When these different zones are decidedly different in their refractive errors, the same average can be obtained by a combination of different elements, so that there may be different observations, two or three of which will give practically the same visual acuity. In such cases, which are rather puzzling, I would like to ask Dr. Beach what he suggests doing. I myself have always suggested trying the different prescriptions at the near point to see which gives the best results there, because, as the pupil contracts, there are fewer zones which have to be averaged, and that correction which will best suit the eye for both far and near will be obtained. Incidentally, an understanding of this point of variability in the pupillary zones is valuable in studying and evaluating the relative validity of different methods of refraction.

DR. I. S. TASSMAN, Philadelphia: Dr. Beach has presented a thorough procedure for refraction. However, nothing has been said about refraction for children. It ought to be emphasized that cycloplegic refraction with atropine should be employed with children up to the age of at least 12 years. The preliminary examination should be carried out as Dr. Beach described, then followed by cycloplegic examination and also a postcycloplegic examination. All of the methods and tests that are mentioned and described can be applied in every case, as Dr. Beach pointed out, with one checking the other. The power of discrimination of the patient should also be evaluated by the examiner. It is important that one recognize the visual as well as the mental alertness of the patient is important, and that should be taken into consideration in determining the best result obtained in that particular patient.

DR. S. JUDD BEACH: Cyclodamia is the name that Dorland Smith gave to a binocular form of descending fogging. The vision is deeply fogged by high convex lenses. Both eyes are exposed at the same time. Three levels of visual acuity are noted as the fog is gradually reduced. At the top level the 20/200 line becomes visible binocularly. This indicates fogging by a + 1.50 sphere in both eyes; at the second level the 20/40 line appears, indicating fogging by + 0.50 spheres; at the lowest level, the 20/20 line is seen. In obtaining the cycloplegic acceptance, textbooks tell one to change spheres, a little plus or a little minus, until 20/20 vision is reached. If in this way 20/20 vision is not obtained, then cylinders should be tried. On the contrary, I feel that the routine I described for noncycloplegic refraction is also best under cycloplegia. First the cylinder and then the sphere should be determined. I was not prepared to have so many persons agree with me. What Dr. Bair added to the discussion about the near point test is true, but, as Dr. Post said, that does not make it any the less desirable to measure the near point in each case. Dr. Pascal raised a significant question concerning the variation in refraction in different areas of the cornea. There is some question as to whether, with the enlarged pupil, the patient averages these different refractive errors or whether, as Dr. Crisp and Dr. Lancaster some time ago suggested, the patient chooses the area he prefers or with which he sees best. I cannot go into that, because it would take a long discussion to explain the optical principles involved, but there are two points of view with regard to that. Of course, Dr. Tassman's contribution about the examination of children is important.

Clinical Notes, Suggestions and New Instruments

"DIASONE" THERAPY OF ACTINOMYCOSIS OF THE JAW

Report of a Case

HARRY L. ARNOLD Jr., M.D.
and
E. R. AUSTIN, M.D.
Honolulu, Territory of Hawaii

In March of this year (1948) Dr. Fernando Latapí of Mexico City demonstrated to one of us (H. L. A.) a case of actinomycosis in which an extensive cutaneous granuloma was healing rapidly, apparently as a result of the oral administration of disodium formaldehyde sulfoxylate diaminodiphenylsulfone ("diasone," Abbott). A similar response had been observed by him in two previously treated patients with this disease. The dose employed was that customarily used in the treatment of leprosy in Mexico: 15 grains (1 Gm.) daily for the first week, 20 grains (1.3 Gm.) daily for the second week and 25 grains (1.6 Gm.) daily thereafter. This is a much larger initial dose than that used in Hawaii (5 grains [0.3 Gm.] a day, three days a week, raised in 5 grain [0.3 Gm.] increments, on those days only, till 25 grains [1.3 Gm.] is reached, and then the same initial dose and the same increments on the alternate days). It is three times as large as the initial dose recommended by the Fifth International (Havana) Leprosy Congress in April of this year. Extensive experience in Guadalajara and in Mexico City indicates, however, that it is not dangerously high.

Fig. 1.—Lesion on July 3, before treatment.

The purpose of this report is to bring these cases, and an additional case of our own, to the attention of American physicians.

REPORT OF A CASE

E. D., a 40 year old Filipino milker of cows, was first seen by one of us (E. R. A.) on July 9, 1948, because of swelling of the soft tissues immediately behind the left ramus of the jaw (fig. 1) following extraction of a tooth about two months previously. Treatment by another physician, consisting of twelve intramuscular injections of penicillin, had had no effect, the mass having increased steadily in size. The patient's temperature was 99.6 F. Roentgenograms showed irregular decalcification of the left side of the mandible; the bony cortex was intact, however, and the process was interpreted by the roentgenologist as secondary to the soft tissue mass. Kolmer, Wassermann and Eagle reactions of the blood were negative.

From The Clinic, Honolulu.

A biopsy of the mass revealed only vascular granulation tissue with suppuration. A second biopsy specimen, from inside the mouth, showed a similar process, in which some amorphous material was found which suggested a fungus colony. Further sections, however, failed to confirm this observation and showed changes which were interpreted as indicative of a mixed tumor of the parotid, with nonspecific infection in the region of the extraction of the tooth.

The patient received penicillin in oil and wax intramuscularly, 300,000 units on June 14, 150,000 units on June 22 and 300,000 units on June 25 and 29 and on July 2. On July 3 the lesion had begun to drain thick pus from several orifices, and the patient was hospitalized and given 600,000 units of penicillin in oil and wax intramuscularly daily until July 9, at which time slight improvement had occurred, all of the external discharge of pus having stopped. On July 12 another biopsy specimen from inside the mouth revealed only nonspecific pyogenic vascular granulation tissue.

On July 12, two fluctuant areas on the surface of the mass, which was at this time approximately 8 cm. in diameter, were deeply incised, and the evacuated pus collected in a Petri dish and examined. Several yellow granules were observed, which proved microscopically to be colonies of Actinomyces.

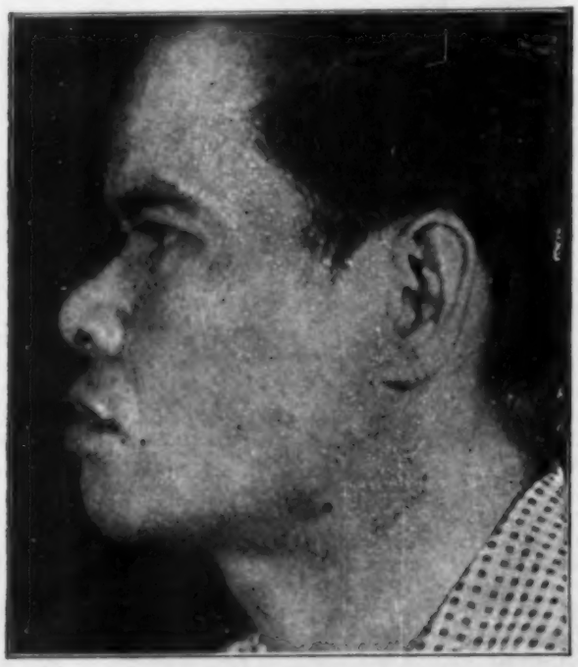

Fig. 2.—Lesion on August 10, at the end of the fourth week of "diasone" therapy.

"Diasone" therapy was begun immediately in a dose of 15 grains (1 Gm.) daily, and the dose was increased each week by 5 grains (0.3 Gm.) daily. No intolerance was reported by the patient. The blood cell counts are shown in the accompanying table. At the end of the first week, both the incisions had healed completely; at the end of the second week, the lesion was still very firm, but the surrounding soft tissue swelling was noticeably diminished; at the end of the third week, the lesion was reduced to about two thirds of its original size and the skin was freely movable over it; at the end of the fourth week (fig. 2) there was only a residual fibrotic nodule, less than one-sixth the size of the original mass, with normal overlying skin except for a few scars. The red cell count had risen to nearly 5,000,000 and the hemoglobin to 16 Gm.

Weekly Blood Cell Counts and Urinary Albumin Determinations During Administration of "Diasone"

Date	Daily "Diasone" Dosage During Previous Week, Gm.	Red Blood Cell Count (Millions/Mm.³)	Hemoglobin		White Blood Cell Count (Thousands/Mm.³)	Polymorphonuclear Cells*	Lymphocytes*	Monocytes*	Eosinophils*	Albumin in Urine
			Gm./100 Cc.	Percentage						
7/12/48	0	4.3	14.0	89.5	13.5	61	25	2	12	Trace
7/20/48	1.0	3.7	13.6	87.0	11.8	59	20	5	16	Trace
7/27/48	1.3	4.7	15.0	96.0	11.7	71	25	0	4	1 plus
8/3/48	1.6	5.0	15.6	100.0	13.7	61	24	0	15	1 plus
8/10/48	1.6	4.8	16.0	103.0	12.0	75	25	0	5	Trace

* Percentage of total.

The initial drop in the red blood cell count may have been due to the hemolytic effect which "diasone" is known to have in certain patients. The prompt return of the cell count to normal without adjuvant therapy of any sort indicates that this effect may be a transitory one.

COMMENT

The response to penicillin in the hospital is in line with previous reports of the effectiveness of this drug in actinomycosis, and suggests that—had the diagnosis been known at that time, so that more confidence could have been reposed in this form of treatment and the dose increased or the schedule prolonged—a cure might have been obtained in this way. However, the decided flare-up of the process after the penicillin therapy was stopped seems to exclude any possibility that this drug participated in the subsequent improvement of the lesion. This improvement began so promptly and progressed so rapidly under "diasone" therapy that it seems reasonable to attribute it to the latter drug.

CONCLUSIONS

Biopsy may be a less satisfactory means of diagnosis in actinomycosis, probably because it is often of necessity relatively superficial, than examination of the purulent discharge for "sulfur granules."

"Diasone" seems worthy of further trial in the treatment of actinomycosis.

881 South Hotel Street.

SUBACUTE BACTERIAL ENDOCARDITIS

Report of a Case of Reinfection

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Los Angeles

The treatment of subacute bacterial endocarditis has been divided historically by most authors into three distinct periods of time. The first encompasses the period before the use of sulfonamide drugs, when it was estimated that the incidence of spontaneous recovery varied between 0 and 1 per cent. The second phase began with the use of sulfonamide drugs, either with or without fever therapy. Lichtman,[1] in an analysis of 704 cases falling in this group, computed the incidence of recovery to vary between 4 and 6 per cent. This was felt to represent a significant percentage increase. Since the advent of penicillin therapy, in the third period, a considerable number of authors have discussed the principles of treatment, the dosages used and the results obtained with penicillin. The percentage of cured patients has increased until it now is estimated to lie between 60 and 80 per cent. Some of the cases have been followed up for as long as thirty-five months after treatment

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Dr. Morley J. Kert, Junior Consultant, Internal Medicine, Wadsworth General Hospital, gave helpful suggestions and criticisms during the preparation of this paper.

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1. Lichtman, S. S.: Treatment of Subacute Bacterial Endocarditis: Current Results, Ann. Int. Med. **19**: 787 (Nov.) 1943.

was concluded.[2] Hunter cited 41 cases of clinical cure, some of which were followed-up for eighteen months after treatment,[3] while Priest, Smith and McGee [4] stated that thirty-five months had elapsed since the treatment in some of their cases.

The purpose of this paper is to report a case of subacute bacterial endocarditis which recurred twenty months after completion of the first course of therapy. The apparent adequacy of the primary treatment, together with the long interval during which the patient was symptom free, make it seem that reinfection, rather than relapse had occurred.

REPORT OF A CASE

First Admission.—A 31 year old white salesman was admitted April 8, 1946, to a hospital, complaining of fatigue and chronic low grade fever of two months' duration. Approximately two months before entry he had had a mild infection of the upper part of the respiratory tract characterized by persistent low grade fever, fatigue, loss of energy and transitory arthralgia of the knees, elbows and back. He took sulfadiazine tablets for three days without relief. Immediately prior to entry, the right calf became painful, tender and swollen and two small red painful nodules appeared on his fingers. Physical examination revealed a well nourished normally developed white man who was not acutely ill. There was a reddish nodule on the palmar surface of the right hand. He had a ticktack rhythm of the heart, a split mitral first sound, but no murmurs were heard. The right calf was exquisitely tender and was ¾ inch (2 cm.) larger in circumference than the left.

Laboratory examination revealed mild anemia, leukocytosis and an elevated sedimentation rate. Two blood cultures were positive for Streptococcus viridans. While the patient was in the hospital cutaneous lesions suggestive of erythema nodosum developed, with petechial lesions of the uvula and electrocardiographic changes suggestive of rheumatic fever. Three weeks after entry an aortic systolic and diastolic murmur appeared, together with a widened pulse pressure. A diagnosis of subacute bacterial endocarditis, presumably on a bicuspid aortic valve, was made. The patient was treated with 800,000 units of penicillin daily for six weeks. After three negative monthly blood cultures and an asymptomatic follow-up period he was discharged as cured.

Second Admission.—The patient remained well until he entered the reporting institution on Feb. 11, 1948, because of a three week history of low back pain. This was deep to the right posterior iliac aspect of the spine. His temperature was noted to be 101 F. rectally. Before entry, while under "pentothal sodium" (sodium 5-ethyl-5-[1-methylbutyl] thiobarbiturate) anesthesia he had received osteopathic manipulation of his back. Exacerbation of his low back pain had resulted. He was also given penicillin therapy during this period, and of interest is the fact that his temperature returned to normal, only to rise when the penicillin therapy was discontinued.

On examination he was seen to be well developed and nourished, but immobilized in bed by his severe low back pain. Positive physical observations were of a slight left-sided cardiac enlargement, a forceful apical beat, an aortic systolic grade 1 murmur, which was transmitted to the neck, and a grade 3 diastolic aortic murmur. This was transmitted to the apex. His blood pressure was 150 systolic and 70 diastolic. The orthopedic consultant observed no local pathologic condition in the back, but did feel that any torsion of the spine aggravated the pain.

Laboratory examination revealed 12,660 white blood cells, with a normal differential count, and 4,100,000 red blood cells, with 86 per cent hemoglobin. The sedimentation rate was 28 mm. in sixty minutes. Four successive blood cultures were positive for S. viridans. The urine, Wassermann reaction of the blood and spinal fluid were normal. Roentgenograms of the back revealed narrowing of the lumbosacral segment with apparent calcification of the nucleus pulposus. There were minimal arthritic changes of the apophyseal joints. There was minimal enlargement of the left ventricular outflow tract shown in roentgenologic examination. An apical abscess of the lower right first molar was found, and culture of the abscess fluid after extraction yielded S. viridans.

The organism isolated by blood culture proved to be sensitive to less than 0.1 unit of penicillin per cubic centimeter by in vitro tests. Patient was given 6,000,000 units of penicillin daily, with return of the elevated temperature to normal within three days. The penicillin was given by intramuscular injection each two hours. After twelve days the dosage was decreased to 3,000,000 units daily. This was continued for twenty days, with a serum penicillin level of 5 units per hundred cubic centimeters. The total penicillin administered was 132,000,000 units in thirty-five days. The blood cultures, temperature and leukocyte count returned to normal shortly after specific therapy was begun and continued at normal levels for the succeeding five months. The sedimentation rate, at the time of writing, had been persistently elevated.

COMMENT

This case presents certain points of particular interest. I feel that the presence of an apical root abscess yielding the same organism as that seen on blood culture indicates the origin of the present valvular infection. This correlates with the work of Okell and Elliot,[5] who observed that 61 per cent of 84 patients experienced transient bacteremia following tooth extraction under general anesthesia. If pronounced gum disease was present, the figure rose to 75 per cent. Of interest is the fact that 12 of the 100 patients cited by these authors had bacteremia before any operative procedure had been done, indicating that transient bacteremia may occur at any time. Rhoads [6] obtained similar data by taking blood cultures at ten minute, three hour and twenty-four hour intervals after tooth extraction. Positive cultures were obtained in 8 of 25 cases. He also cited cases of patients with pronounced gingivitis who had positive blood cultures following the chewing of mint candies.[6] Correlation of this and other data has led most investigators to list the teeth and gums as the primary focus of infection in the majority of cases of bacterial endocarditis. This case is no exception.

It is not clearly established whether a previously inadequate course of penicillin therapy will alter the penicillin resistance of an organism to further treatment. The decided sensitivity of the organism in the aforementioned case raises the question whether this indicates a reinfection or a relapse. Several authors, among them Bloomfield and Halpern [7] and Flippen and his co-workers,[8] expressed the belief that inadequate courses of therapy, particularly if carried out for long periods of time, tend to increase the resistance of the organism to penicillin. Particularly would this be true if the second course were not given promptly after the relapse developed. The possibility that my patient might have a recurrent infection, therefore, further complicated the determination of how much penicillin to be given. Because of technical difficulties I was not able to secure an immediate report of the penicillin sensitivity of the organism. Consequently it was decided to begin with 6,000,000 units of penicillin per day. This was decreased when the penicillin sensitivity was obtained. The pronounced sensitivity displayed in this case, however, would seem to be corroborative evidence in favor of a reinfection.

Before determining that reinfection has occurred, one must first define what constitutes a cure. Goerner, Geiger and Blake [9] recognized this problem when they stated that spontaneous remissions might occur which may last for weeks.

2. (*a*) Flippin, H. F.; Maycock, R. L. Murphy, F. D., and Wolferth, C. C.: Penicillin in the Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **129**: 841 (Nov. 24) 1945. (*b*) Massel, B. F., and Jones, T. D.: Subacute Bacterial Endocarditis, New England J. Med. **235**: 605 (Oct. 24) 1945. (*c*) Thill, C. J., and Meyer, O. O.: Experience with Penicillin and Dicoumarol in Treatment of Subacute Bacterial Endocarditis, Am. J. M. Sc. **213**: 300 (March) 1947.

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6. Rhoads, P. S.: Subacute Bacterial Endocarditis: Etiological Considerations and Prophylaxis, M. Clin. North America **32**: 176 (Jan.) 1948.

7. Bloomfield, A. L., and Halpern, R. M.: Penicillin in Subacute Bacterial Endocarditis, J. A. M. A. **129**: 1135 (Dec. 22) 1945.

8. Flippin, H. F.; Maycock, R. L., and White, W. L.: The Treatment of Subacute Bacterial Endocarditis, M. Clin. North America **30**: 1233 (Nov.) 1946.

9. Goerner, J. R.; Geiger, A. J., and Blake, F. G.: Treatment of Subacute Bacterial Endocarditis with Penicillin: Report of Cases Treated Without Anticoagulant Agents, Ann. Int. Med. **23**: 491, 1945.

Permanent disappearance of symptoms was rarely reported without specific treatment. A large number of patients have been reported to have become asymptomatic after being treated with small doses of penicillin, only to display a recurrence of symptoms when the penicillin therapy was discontinued. Because of this, it was felt that time was the only criterion of a permanent cure. Numerous authors have presented the same point of view.[10] Hunter stated that if relapses occur, they almost always develop in the first two weeks after therapy is stopped.[3] To avoid this, he advocated intensive therapy. Christie reported 147 patients treated under the English clinical trials committee and stated that when relapses occur they do so within thirty days after treatment and are extremely rare after fifty days. This principle was used to evaluate the efficacy of varied forms of treatment.[11] If their patients remained asymptomatic for fifty days after treatment, they were considered cured. There was relapse in only 1 of their cases after this time, with symptoms recurring sixty days after treatment. This was considered to be a reinfection, inasmuch as a different organism was obtained on relapse than had been seen on initial infection. Gefter and his co-workers [12] gave a slightly more conservative definition. They expressed the belief that twelve months should be considered the critical period. If a patient survives this period without a further development of symptoms, he is considered cured. Prior to the use of penicillin there were extremely few reports of patients living this long in remission. Therefore, if there is clinical or bacteriologic evidence of subacute bacterial endocarditis after this time, it is considered that the patient has a reinfection.

In view of the multitude of reports of clinical and bacteriologic cures of bacterial endocarditis which have appeared in the last few years, there are relatively few reported reinfections. Geiger treated 1 patient in whom the disease occurred six months after initial treatment,[13] and Paul and his co-workers [14] reported a case which they felt recurred seventeen months after the initial treatment course. Christie reported the aforementioned case. Cannady [15] treated a patient with reinfection occurring twelve months after the first attack. Thill and Meyer reported a patient who had a reinfection one year after treatment. He had been well and working until after a dental extraction clinical and bacteriologic evidence of reinfection was observed.[2e]

It is expected that cases of this type will become more frequent in the future. With the occurrence of an increasing number of cures of a previously uniformly fatal disease, the opportunity for reinfection will be heightened. Whether a valve additionally scarred following the eradication of a mycotic vegetation will be more susceptible to further infection than one scarred merely as a result of rheumatic fever or a congenital lesion is not at present known. It is felt, however, that the case presented herein is an illustration of a patient who was cured of his disease by means of penicillin and who experienced a reinfection at a later date.

It has been recommended that follow-up studies of all cured patients be done to forestall this possibility. Priest, Smith and McGee utilized weekly examinations of the white blood cells, sedimentation rate and blood cultures for the first month after treatment, semimonthly checks for the next six months and monthly examinations thereafter. Others have expressed the belief that the temperature and sedimentation rate are the most important observations. Jones and Tichy [16] reviewed the literature and found no active cases of endocarditis without an elevation of the temperature and sedimentation rate.

10. Scheifley, C. H., and Hagedorn, E. B.: Treatment of Subacute Bacterial Endocarditis: A Report of Forty Cases, Proc. Staff Meet., Mayo Clin. **22**: 527 (Nov. 12) 1947. Clark, W. H.; Bryner, S., and Rantz, L. A.: Penicillin Resistant Non-Hemolytic Streptococcal Subacute Bacterial Endocarditis, Am. J. Med. **4**: 671 (May) 1948.
11. Christie, R. V.: Penicillin in Subacute Bacterial Endocarditis, Brit. M. J. **1**: 381 (March 16) 1946.
12. Gefter, W. I.; Maher, I. E., and Dworin, M.: Treatment of Subacute Bacterial Endocarditis, Clinics **5**: 58 (June) 1946.
13. Geiger, A. J.: Experiences in the Treatment of Subacute Bacterial Endocarditis with Penicillin, Am. Heart J. **33**: 736 (May) 1947.
14. Paul, O.; Bland, E. F., and White, P. D.: Bacterial Endocarditis, New England J. Med. **237**: 349 (Sept. 4) 1947.
15. Cannady, E. W.: The Successful Use of Penicillin in the Treatment of Subacute Bacterial Endocarditis, Illinois M. J. **93**: 94 (Feb.) 1948.
16. Jones, S. H., and Tichy, F. E.: Bacterial Endocarditis Treated with Penicillin, New England J. Med. **236**: 729 (May 15) 1947.

There are many variations of the aforementioned procedures which can be used. The primary point of importance would seem to be the use of one type of follow-up period to insure freedom from reinfection. This would be of most importance the first few months after treatment is concluded, but should also be done periodically thereafter.

SUMMARY AND CONCLUSIONS

A case of subacute bacterial endocarditis is presented which is believed to be an example of reinfection. Salient features of the case involving the portal of entry, sensitivity of the organism and response to treatment are outlined. A short discussion of the concept of reinfection in subacute bacterial endocarditis is presented. It is felt that one year should be selected as the dividing line between relapse and reinfection. Most cases will show a recurrence of symptoms in the first or second month after treatment is ended. It is believed that periodic follow-up studies should be done on all patients cured of subacute bacterial endocarditis.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following report on the recommendation of its Consultants on Electroencephalography. The consultants are: Drs. Percival Bailey, Edward J. Baldes, Hallowell Davis and Frederic A. Gibbs.

HOWARD A. CARTER, *Secretary.*

TENTATIVE MINIMUM REQUIREMENTS FOR ACCEPTABLE DIRECT READING ELECTROENCEPHALOGRAPHS

The following requirements are based on recommendations drawn up by the American Electroencephalographic Society (1947). The recommendations of the Society were intended as recommendations to manufacturers, not as minimum requirements. In the following requirements it should be noted that certain items are specified herewith as minimum requirements for Council acceptance; others are stated as the recommendations of the American Electroencephalographic Society for desirable additional features for higher standards of performance.

A. NUMBER OF CHANNELS

Portable equipment may include a minimum of two channels. Clinical laboratory equipment shall include not less than four channels. For research equipment an even larger number of channels is usually desirable.

B. ELECTRICAL AND MECHANICAL SPECIFICATIONS FOR EACH RECORDING CHANNEL

1. *Linearity of Response.*—The deflection appearing in the record shall be directly proportional to the voltage applied to the input of the apparatus to within 10 per cent (or ½ mm., whichever is larger) up to an amplitude of linear deflection not less than 1 cm. in each direction from the base line (i. e., 2 cm. over all).

2. *Amplification.*—(*a*) When the controls are set for maximum amplification an input voltage change of 5 microvolts (5μv) shall give a deflection of not less than 2 mm. This requirement in conjunction with section B1 implies a sensitivity at the highest gain setting of not less than 2.5 μv per millimeter.

(*b*) The ratio between the maximum deflection proportional to the input voltage and the minimum visible deflection shall be not less than 40 to 1. For example, if a 1 cm. deflection is obtained from 160 microvolts input the deflection for 4 microvolts input must be visible at the same gain setting.

(*c*) The total attenuation available shall be not less than 1,000 to 1. The American Electroencephalographic Society recommends that there should be two controls of amplification. The principal control should have increasing steps of not more than 100 per cent per step and should provide an over-all attenuation of at least 25 to 1. The second gain control should pro-

vide continuous adjustment for equalization of the gain in the various channels.

3. *Frequency Response.*—(*a*) The over-all frequency response of the system shall be such that between 1 and 60 cycles per second the deflections at all frequencies shall be within 10 per cent of the average of the maximum and the minimum deflections within this range.

(*b*) Over-all time constant (R. C.), without low frequency cut-off filters, should not be less than 0.2 second. This implies a square wave response which declines to 0.37 of its peak value in 0.2 second.

(*c*) The American Electroencephalographic Society recommends the provision of both low frequency cutoff filters and high frequency cutoff filters.

(*d*) The American Electroencephalographic Society recommends that there should be no significant distorting resonance in the system outside of the frequency range of 1 to 60 cycles per second.

4. *Coupling of Controls.*—The American Electroencephalographic Society recommends that the operation of any one control should not alter the effective setting of any other control by more than 15 per cent.

5. *Noise Level.*—With the input short-circuited and with the controls set to meet the requirement of section 3 (*a*) no deflections greater than that produced by an input voltage of 2 microvolts (peak to peak) shall appear oftener than once a second on the average.

6. *Effect of Line Voltage Fluctuations.*—A line voltage fluctuation amounting to 5 per cent above or below the voltage recommended by the manufacturer as normal operating voltage shall not produce a deflection in the record greater than that produced by an input voltage of 2 microvolts (peak to peak).

7. *Discrimination.*—"Discrimination" here refers to the ratio of a potential difference applied between ground and the input terminals connected together (for a given deflection) to the potential difference applied between the input terminals for the same deflection. The discrimination of the instrument shall be at least 1,000 to 1. The American Electroencephalographic Society recommends even more discrimination, particularly in portable apparatus.

8. *Limitation of Arc Distortion.*—The maximum arc distortion shall be not more than that produced by a pen 10 cm. long.

C. Relationships Between Channels

1. *Coupling Between Channels.*—When the controls in all channels are set for equal sensitivity a potential difference applied to the input of one channel only shall not produce a deflection in any other channel greater than 1 per cent of that in the channel to which the potential difference is applied.

2. *Similarity of Channels.*—The American Electroencephalographic Society recommends that the several channels shall be as nearly identical as possible and suggests the following practical criterion: When all principal gain and filter controls are set to the same positions and the channels are matched for sensitivity by setting the appropriate fine controls and identical input signals are applied simultaneously to the inputs, then all of the channels should give records that are superimposable within 10 per cent or ½ mm., whichever is larger.

D. Recorder

1. *Recording Surface Travel.*—The recording surface shall travel from the operator's right to his left and shall be visible for a distance of not less than 60 cm. to the left of the recording line.

2. *Recording Surface Speed.*—The standard speed for recording shall be 30 mm. per second ±2 per cent. The American Electroencephalographic Society recommends that one faster and one slower speed (each at an integral ratio to the standard) be provided and that these speeds be selectable while the recorder is in operation.

3. *Recording Line.*—The width of the recorded line shall be not more than ½ mm. in all directions of travel.

4. *Spacing and Registration of Recording Lines.*—(*a*) At zero deflection all the recorder writing points shall lie within ±0.5 mm. of a line perpendicular to the time axis of the record in the plane of the record.

(*b*) The spacing between writing points at zero deflection shall be not less than the maximum peak to peak recordable deflection.

(*c*) The American Electroencephalographic Society recommends that the maximum spacing of the recorders shall be not more than 35 mm. It also recommends that unless satisfactory accuracy is guaranteed by the manufacturer each recorder should be adjustable (to the accuracy specified above) in respect to (1) registration in line with the other recorders, (2) lateral spacing between recorders and (3) pressure on the recording surface (accuracy not specified).

E. Construction and General Requirements

1. *Selector Switches.*—The American Electroencephalographic Society recommends that selector switches with at least 16 contacts should be provided at the input of each channel.

2. *Shielding and Grounding.*—The input leads from an appropriate distributor panel to the input selector switches shall be shielded and the shield(s) shall be securely attached to the common ground. Leads for the AC power supply shall also be shielded and the shield securely attached to the common ground.

3. *Electrode Connectors.*—The American Electroencephalographic Society recommends that input leads to connect the electrodes to the distributor panel should be provided and should be fitted with appropriate clips and plugs to suit individual requirements.

4. *Calibrator.*—(*a*) A calibrating circuit shall be provided at the input of the amplifiers. This circuit shall provide an input voltage of rectangular wave form in single pulses with an accuracy (including any transients) of ±5 per cent of the indicated voltage(s).

(*b*) The American Electroencephalographic Society recommends the following values for the indicated voltages of the calibrator: 5, 10, 20, 50, 100, 200, 500, 1,000 V.

5. *Meters.*—The American Electroencephalographic Society recommends that suitable meters or suitable test points for connecting meters should be provided to measure (*a*) the voltage of the calibration battery, (*b*) the voltage of all A and B batteries used in the amplifiers, and (*c*) the resistance or impedance of any two electrodes attached to the patient. A polarity reversing switch should be provided to make it possible to check the effect of electrode polarization on measurements of resistance.

6. *Noise and Vibration.*—The construction of the apparatus shall be such that no external insulation from mechanical vibration or from noise within the apparatus is required to prevent damage or to avoid spurious deflections in the record. The American Electroencephalographic Society recommends that the noise and vibration should be such that its effect on the patient will be negligible.

7. *Finish.*—All exposed surfaces should be resistant to the action of sodium chloride solution and to any recording fluids that are recommended by the manufacturer.

8. *Labels.*—(*a*) The electroencephalograph shall have a name plate giving the manufacturer's name, the serial number, the voltage and frequency (or frequencies) of the power supply and the power consumed by the electroencephalograph.

(*b*) All test points, dials, switches, etc., shall be clearly and appropriately labeled.

(*c*) The American Electroencephalographic Society recommends that a pilot light be provided to indicate when any power supply is switched on.

9. *Continuity of Operation.*—(*a*) The requirements specified in sections B1, 2, 3, 4, 5, 6 and 7 shall be attained within fifteen minutes of switching on and shall be maintained for a period of 24 hours of continuous operation.

(*b*) One hour of continuous recording at a speed of 30 mm. per second shall be possible without replacement of recording materials.

10. *Life.*—The requirements specified in sections B1, 2, 3, 4, 5, 6 and 7 shall be guaranteed by the manufacturer for a period of 1,000 hours' use or one year from date of shipment, which-

ever is less, exclusive of battery replacements or recharging and of tubes which may be guaranteed by their manufacturer.

11. *Safety.*—The apparatus shall conform in all respects to the recommendations of the Underwriters' Laboratory regarding the safety of the patient and the operator and also regarding fire hazard. There shall be no direct current coupling between the input grids of an amplifier and the patient. There should be no possibility of high voltage reaching the electrodes attached to the patient.

12. *Portable Apparatus.*—(*a*) In portable apparatus each unit of the equipment should be limited to a weight not exceeding 40 pounds.

(*b*) The visibility of the record need not meet the requirements of specification D1. Otherwise portable equipment shall fulfil the requirements of construction, performance, life, etc., as listed.

F. Information and Instructions

Adequate instructions shall be provided for the proper care and upkeep of the instrument. The American Electroencephalographic Society recommends that a functional wiring diagram of the amplifier circuits together with appropriate service information be supplied with each apparatus. It is highly desirable that a complete wiring diagram with schedule of values be provided.

G. Marketing and Advertising

Rules of the Council on Physical Medicine shall be adhered to by manufacturers of acceptable electroencephalographs.

REPORT OF THE COUNCIL

The Council on Physical Medicine has authorized publication of the following report. Howard A. Carter, *Secretary.*

M.S.A. PNEOPHORE ACCEPTABLE

Manufacturer: Mine Safety Appliances Company, Braddock, Thomas and Meade Streets, Pittsburgh 8.

The M.S.A. Pneophore is an apparatus for administering oxygen by intermittent positive pressure where breathing has been arrested or impaired. It consists of the following:

1. A high pressure reducing valve which reduces cylinder pressure to 3.4 atmospheres (2,600 mm. of mercury). A gage to indicate the oxygen cylinder pressure is part of this assembly.
2. A low pressure regulator equipped to reduce the pressure from 50 pounds per square inch to an adjustable pressure range from 0 to 30 centimeters of water (0 to 22 mm. of mercury).
3. A gage calibrated in centimeters of water to indicate the pressure being delivered.
4. A 6 foot (183 cm.) length of rubber tubing.
5. A differential pressure valve which converts a continuous positive pressure into an intermittent positive pressure, thus acting as an automatic respirator.
6. Two positive pressure face pieces, each with a 4 inch (10 cm.) length of tubing attached.

M.S.A. Pneophore

The apparatus is contained in a carrying case (optional) that is constructed of plywood and fiber with metal-reinforced corners and measures 41 by 30 by 20 cm. (16 by 12 by 8 inches). It weighs 3.7 Kg. (8½ pounds); the shipping weight is 5.4 Kg. (12 pounds).

After consideration of the available evidence the Council concluded that the apparatus is acceptable for use in medical institutions under the direction of a physician. It may be used in cases of respiration failure—e. g., poliomyelitis—for a short period of time (one hour or less) as emergency equipment under the direction of a physician. Because evidence at hand was not sufficient to establish its usefulness as an emergency respirator by fire departments and rescue squads or as a respirator for prolonged use in cases of infantile paralysis, it was not recommended for these purposes. With these reservations, the Council on Physical Medicine voted to include the M.S.A. Pneophore in its list of accepted devices.

Council on Foods and Nutrition

THE VITAMIN B COMPLEX

C. A. ELVEHJEM, Sc.D.
Madison, Wis.

This paper was prepared at the request of the Council and is one of a series appearing in The Journal. Later the entire series will appear in book form as the Council's Handbook of Nutrition. James R. Wilson, M.D., *Secretary.*

The group of dietary factors, the vitamin B complex, is included in the larger class of water-soluble vitamins because, like all vitamins, they are required by the body in small amounts and because the individual chemical compounds are soluble in water although the degree of solubility varies from the sparingly soluble riboflavin to the readily soluble choline. These are the main characteristics common to the individual vitamins because their functions in the living cell may differ greatly and their chemical structure may vary from the simple configuration of nicotinic acid to the more complex molecular structure of thiamine and riboflavin. The vitamin B complex is usually differentiated from the other water-soluble vitamins, such as vitamin C and related factors, on the basis of the source material used in early isolation work and the kind of experimental animals employed for the assay.

No attempt will be made to cover in this short summary the vast amount of literature which is accumulating on the water-soluble vitamins. A symposium entitled "The Vitamins," [1] published by the American Medical Association in 1939, includes a survey of the facts known at that time. This chapter is a revised form of chapter 11 in the first "Handbook of Nutrition" [2] and will include only a general summary of the more significant facts, and reference will be made to original papers only when they have been published within the past few years. Since this review will stress the nutritional importance of these vitamins, the description of the clinical aspects of the deficiency diseases resulting from their deficiency will of necessity be limited. A recent publication by Jolliffe, Tisdall and Cannon [3] includes a description of the clinical symptoms.

The B complex now is known to consist of at least a dozen separate factors, ten of which can be obtained in crystalline form. Each factor will be discussed separately and in more or less chronologic order of its recognition and identification.

THIAMINE

Thiamine hydrochloride is a white crystalline substance readily soluble in water, possessing a nutlike and salty taste and a yeastlike odor. The empiric formula is $C_{12}H_{18}N_4OSCl_2$, and the compound has the structural formula shown in figure 1.

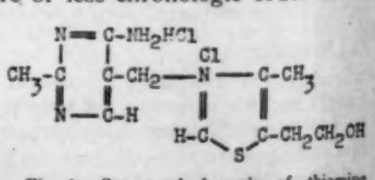

Fig. 1.—Structural formula of thiamine hydrochloride.

1. The Vitamins, Chicago, American Medical Association, 1939.
2. Handbook of Nutrition, Chicago, American Medical Association, 1943.
3. Jolliffe, N.; Tisdall, F. F., and Cannon, P. R.: Handbook on Clinical Nutrition, to be published.

It is rapidly destroyed in neutral or alkaline solutions because of hydrolytic cleavage into its constituent pyrimidine and thiazole rings, but in acid solutions it can be sterilized for half an hour at 120 C. without appreciable loss of activity. In the dry form it is very stable and is not readily destroyed by oxidation. Its activity is rapidly destroyed by sulfite, a fact which may explain the loss of thiamine during the sulfuring of fruits. This vitamin also seems to be very rapidly destroyed in dehydrated meats and vegetables when the moisture content is approximately 5 per cent.

In foods and in tissues it occurs both in the free form and as thiamine pyrophosphate or cocarboxylase. In the latter form it functions in the living cell as a coenzyme in carbohydrate metabolism, especially in the metabolism of alpha-keto acids. In thiamine deficiency the utilization of carbohydrate is incomplete and pyruvic acid accumulates in the tissues, a condition which is used in determining thiamine insufficiency. Many of the symptoms which have been observed in beriberi may be related to faulty carbohydrate metabolism, although it is still difficult to differentiate an uncomplicated thiamine deficiency from multiple deficiencies. Some of the nerve lesions which have been described in experimental animals suffering from polyneuritis are certainly related to a deficiency of riboflavin, but there is also good evidence that a lack of thiamine may directly cause neuropathy.

The variety of symptoms seen in human beings has been summarized by Williams and Spies,[4] Jolliffe [5] and Jolliffe and his co-workers.[5] Wilder [6] has pointed out that the type of symptoms produced depends to a considerable extent on the rate at which the deficiency develops, but in all cases the subjects become depressed, irritable, quarrelsome, uncooperative and fearful. A relationship between thiamine deficiency and cardiac function has been recognized for many years, and Blankenhorn and his co-workers [7] have recently suggested seven criteria for the diagnosis of "beriberi heart." Anemia of the hyperchromic type has also been described in a number of thiamine-deficient patients.

The Food and Nutrition Board of the National Research Council recommends 1.2 to 1.8 mg. as the daily thiamine allowance for the average adult man. The minimum daily requirement as established by the United States Food and Drug Administration is 1 mg. The requirement is increased in periods of active growth and during pregnancy and lactation. Pathologic conditions, such as fevers and hyperthyroidism, in which there is a general increased metabolism, also increase the requirement. The effect of external temperature on the thiamine requirement of experimental animals has been given considerable attention. Mills [8] originally reported that rats need twice as much thiamine per unit of food at 91 F. as at 65 F. However, in more recent work by Kline, Friedman and Nelson [9] in which suboptimal levels of thiamine were used, evidence was presented to show that as the environmental temperature is increased, the daily requirement for thiamine is decreased.

Diets rich in fat have a definite sparing action on the requirement of thiamine in both rats and dogs. This is undoubtedly because fat metabolism does not require cocarboxylase. The human diet may rarely undergo sufficient change in fat content to alter materially the thiamine requirement. Cahill,[10] studying the urinary excretion of thiamine in human subjects, could observe no increase when part of the carbohydrate was replaced by fat.

The two commonest methods in use today for the quantitative estimation of thiamine are the thiochrome method and the yeast fermentation method. The detailed procedures are given in *Biological Symposia*.[11] The rat assay procedure is still recognized as the official method and is described in the "Pharmacopeia of the United States," thirteenth revision.

TABLE 1.—*Vitamin Content of a Few Typical Foods*

Foods*	Thiamine†	Riboflavin†	Niacin†	Pantothenic Acid‡	Vitamin B6‡	Biotin‡	Folic Acid‡
Apples	0.04	0.02	0.2	0.05	0.03	.....	....
Bananas	0.09	0.06	0.6	0.18	0.30	.....	0.01
Bread							
White (unfortified)	0.08	0.13	0.8	0.40	0.20	.....	....
White (fortified)	0.24	0.15	2.2	0.40	0.10	.....	....
Cabbage	0.07	0.06	0.3	0..8	0.29	.....	0.01
Carrots	0.07	0.06	0.5	0.24	0.19	0.002	0.01
Cheese	0.01	0.50	0.1	0.35	0.20	0.002	....
Cornmeal, degerminated	0.15	0.06	0.9	....	0.25	.....	0.02
Eggs, whole fresh	0.12	0.34	0.1	2.70	....	0.025	0.01
Meat:							
Beef	0.12	0.15	5.2	1.10	0.40	0.004	0.02
Pork loin	1.04	0.20	4.4	1.50	0.60	0.005	0.01
Poultry, chicken or turkey	0.10	0.18	8.0	0.90	0.20	0.01	....
Liver, pork or beef	0.27	2.80	16.1	5.20	0.80	0.1	0.08
Milk, whole fluid	0.04	0.17	0.1	0.30	0.07	0.005	....
Oatmeal	0.65	0.14	1.1	1.30	0.15	.....	0.03
Oranges	0.08	0.03	0.2	0.2	....	.....	0.01
Peas, fresh	0.30	0.18	2.1	0.60	0.05	0.002	0.03
Peanuts, roasted	0.30	0.16	16.2	2.5	0.30	.....	....
Potatoes	0.11	0.04	1.2	0.40	0.16	.....	0.01
Spinach	0.12	0.24	0.7	0.7	0.08	0.002	0.18
Tomatoes	0.06	0.04	0.6	0.37	0.07	0.002	0.01
Turnips	0.06	0.06	0.5	0.25	0.10	0.002	....
Yeast, Brewers' dry	9.69	5.45	36.2	20.00	2.90	0.2	0.7
Wheat, whole	0.56	0.12	5.6	1.30	0.40	0.035	0.05

* Edible portion.
† Values are given in milligrams per hundred grams.
‡ Values for pantothenic acid, pyridoxine (vitamin B6), biotin and folic acid are based on data from only a limited number of samples. Some of the values may be low because of incomplete liberation of the vitamin. This is especially true in the case of pantothenic acid. For example, Nielands and Strong [8a] found 3 mg. in 100 Gm. of spinach after maximum liberation and only 0.7 mg. by the old method. Dried yeast was observed to contain 40 mg. and fresh eggs 5.0 mg.

In table 1 are presented figures for the vitamin content of a few typical foods. It is evident that only a few foods can be classified as rich sources of thiamine; they include peas, beans, oatmeal, whole wheat and enriched flour and bread, lean pork and peanuts. However, one must not overlook the staple foods, such as milk, vegetables and fruits, which may contribute appreciable amounts of thiamine in the diet although the amount per unit of weight is relatively low. It is well known that significant amounts of thiamine may be lost during the preparation of foods, because of the fact that the vitamin is readily soluble in water and easily destroyed by moist heat. Under normal conditions there is probably little destruction of thiamine in the digestive tract, although intestinal disturbance may seriously retard the absorption of this vitamin.

4. Williams, R. R., and Spies, T. D.: Vitamin B_1 (Thiamin) and Its Use in Medicine, New York, The Macmillan Company, 1938.
5. Jolliffe, N.: Recent Advances in Clinical Applications of the B Vitamins, J. Am. Dietet. A. **17**: 5 (Jan.) 1941.
6. Wilder, R. M.: Nutritional Problems as Related to National Defense, Am. J. Digest. Dis. **8**: 243 (July) 1941. Williams, R. D., and Mason, H. L.: Further Observations on Induced Thiamine (Vitamin B_1) Deficiency and Thiamine Requirement of Man, Proc. Staff Meet., Mayo Clin. **16**: 433 (July 9) 1941.
7. Blankenhorn, M. A.; Vilter, C. F.; Scheinker, I. M., and Austin, R. S.: Occidental Beriberi Heart Disease, J. A. M. A. **131**: 717 (June 29) 1946.
8. Mills, C. A.: Vitamin and Protein Requirements at Different Temperatures, Am. J. Physiol. **133**: 390 (June) 1941; Environmental Temperatures and Thiamine Requirements, ibid. **133**: 525 (July) 1941.
9. Kline, O. L.; Friedman, L., and Nelson, E. M.: The Effect of Environmental Temperature on Thiamine Requirement of the Rat, J. Nutrition **29**: 35 (Jan.) 1945.
10. Cahill, W. M.: Urinary Excretion of Thiamine on High Fat Diets, J. Nutrition **21**: 411 (April) 1941.
11. Kline, O. L., and Friedman, L.: Micro-Biological Assay Methods of Thiamine, Biological Symposia **12**: 65-85, 1947.

The possible availability of thiamine synthesized by the bacterial flora of the gastrointestinal tract must not be overlooked, although it appears that less thiamine is produced than some of the other B vitamins.[12] It is also important to mention that the ingestion of live yeasts may render thiamine consumed in other foods unavailable for human beings (Parsons, Williamson and Johnson[13]). Severe thiamine deficiency can be produced in mice by feeding pyrithiamine, the pyridine analogue of thiamine (Woolley and White[14]), but the deficiency can be overcome by administration of an excess amount of thiamine.

Recently a factor destructive of vitamin B_1 has been found in raw fish. Green, Carlson and Evans[15] observed a type of paralysis in foxes fed diets containing 20 per cent fresh carp and identified the condition as a thiamine avitaminosis analogous to Wernicke's disease. Further studies[16] on the mechanism of inactivation point to an enzymatic destruction. Nonenzymatic thiamine-destroying factors have been found in seeds and in fern (Pteris aquilina) by Weswig, Freed and Haag.[17]

RIBOFLAVIN

Riboflavin is a practically odorless orange-yellow crystalline compound, which in water solution shows a characteristic yellow-green fluorescence. The empiric formula is $C_{17}H_{20}N_4O_6$, with the structural formula as shown in figure 2.

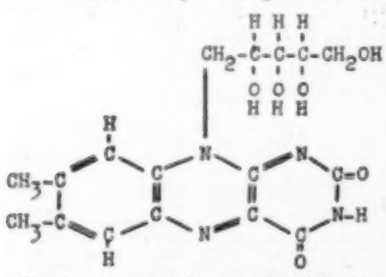

Fig. 2.—Structural formula of d-riboflavin.

This vitamin is rather heat stable, especially in acid mediums, but extremely labile when exposed to light. In nature riboflavin may occur as such, as riboflavin phosphate or as a constituent of specific flavoproteins. These flavoproteins function as important enzymes in tissue respiration. Enzymes known to contain riboflavin include cytochrome reductase, d-amino acid oxidase and xanthine oxidase.[18] A definite reduction in the tissue concentration of the latter enzymes has been observed in riboflavin-deficient animals.[19] Aside from retarded growth in young animals, other symptoms include dermatitis and cataract in rats and characteristic paralysis in chicks. Work by Baum, Michaelree and Brown[20] indicates that the incidence of cataract in rats is increased if the diet supplies a small amount (1 to 2 micrograms daily) of riboflavin. Phillips and Engel have shown a specific neuropathologic condition of the main peripheral nerve trunks in chicks on low riboflavin rations. Similar changes were not observed in the rat until the riboflavin deficiency was aggravated by an increased fat content of the diet.[21] Both acute and chronic riboflavin deficiency has been studied in dogs.[22] On a diet very low in this vitamin a characteristic collapse syndrome and sudden death are observed in six to eight weeks. Prolonged subsistence on a diet low in riboflavin leads to neurologic abnormalities accompanied with myelin degeneration of peripheral nerves and the posterior columns of the spinal cord. Street, Cowgill and Zimmerman[22] have shown that opacities of the cornea may occur in the dog as well as in the rat.

Severe riboflavin deficiency has been produced in the monkey with no evidence of corneal changes.[23] The symptoms include lack of growth, dermatitis and anemia. Warkany and Schraffenberger[24] have described congenital defects and malformations of the skeleton of rats due to a low intake of riboflavin during the gestation period.

In human beings the symptoms include inflammation of the lips, fissures at the corners of the mouth, glossitis, dermatitis and vascularizing keratitis.[25] The ocular symptoms first described by Sydenstricker and his co-workers[26] appear to be constant and may appear before other symptoms of the deficiency. There is still considerable difficulty in distinguishing the glossitis or riboflavin deficiency from that of pellagra, pernicious anemia or iron deficiency and in distinguishing ocular ariboflavinosis from other conditions involving corneal vascularization.

The riboflavin content of foods may be determined by measuring the growth response obtained in chicks or rats maintained on basal rations low in the vitamin, but the more rapid microbiologic method of Snell and Strong[27] is now used extensively. Chemical methods involving measurement of fluorescence are also being used.[28] Riboflavin is widely distributed in plant and animal materials. Liver, milk and green leafy vegetables may be considered the best and most reliable sources in the human dietary. Seeds, which are so important as a source of thiamine, are poor sources of riboflavin.

The Food and Nutrition Board recommends 1.8 mg. of riboflavin as the daily allowance for men, and the Food and Drug Administration has accepted 2 mg. a

12. (*a*) Najjar, V. A., and Holth, L. E., Jr.: The Biosynthesis of Thiamine in Man, J. A. M. A. **123**: 683 (Nov. 13) 1943. (*b*) Denko, C. W.; Grundy, W. E.; Wheeler, N. C.; Henderson, C. R.; Berryman, G. H.; Friedemann, T. E., and Youmans, J. B.: The Excretion of B-Complex Vitamins by Normal Adults on a Restricted Intake, Arch. Biochem. **11**: 109 (Sept.) 1946.

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15. Green, R. G.; Carlson, W. E., and Evans, C. A.: A Deficiency Disease in Foxes Produced by Feeding Fish, J. Nutrition **21**: 243 (March) 1941.

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27. Snell, E. E., and Strong, F. M.: A Microbiological Assay for Riboflavin, Indust. & Engin. Chem. (Anal. Ed.) **11**: 346 (June) 1939.

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day as the minimum daily requirement. The limited values in table 1 show that one serving of liver will adequately meet the daily allowance, that 1 quart of milk will supply the minimum requirement and that one serving of cheese or eggs will supply one fourth of the daily requirement. There is also considerable evidence for the bacterial synthesis of riboflavin in the intestinal tract and that some of this riboflavin can be utilized. Mannering and his co-workers [29] observed that with suboptimal intakes of riboflavin rats receiving a diet high in dextrin or starch grew better than those receiving sucrose-containing diets. When the diet was high in lactose the riboflavin excretion in the feces was many times the dietary intake. Denko and his co-workers [12b] observed the fecal excretion in human subjects to be three times greater than the intake during periods in which there was a low riboflavin intake. Hathaway and Lobb [30] observed a greater excretion when their subjects consumed natural foodstuffs than when they received purified diets, although the intake was the same. Sure and Dichek [31] have demonstrated, in the case of rats, that riboflavin has a pronounced beneficial effect on the economy of food utilization for the synthesis of body tissues. In this connection it is interesting to note that Murlin and his co-workers [32] reported that the biologic value of proteins in bread is improved in the presence of extra B vitamins.

NICOTINIC ACID

Nicotinic acid occurs as white needle-like crystals, is nonhygroscopic and stable in air and has the empiric formula $C_6H_5O_2N$. The structural formula of both the acid and the physiologically active amide are shown (fig. 3).

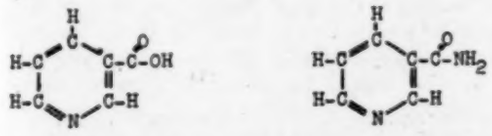

Fig. 3.—Structural formula of nicotinic acid (niacin) (left) and nicotinic acid amide (niacin amide) (right).

The sensation of flushing and erythema of the skin which is often observed on administration of nicotinic acid is not produced by nicotinic acid amide. Nicotinic acid is a comparatively weak acid, and its alkaline salts in solution show a slightly alkaline reaction. It is stable to autoclaving temperatures when in solution and shows no loss of activity when exposed to dry heat. Owing to numerous objections to the term nicotinic acid, niacin and niacin amide are used as synonyms for the acid and amide.

In the body nicotinic acid functions as a component of two important coenzymes, coenzyme I, or cozymase, and coenzyme II, which are concerned in both glycolysis and respiration.[33] The structure of the two coenzymes is similar, differing only in the number of phosphoric acid units. Coenzyme I is a diphosphopyridine nucleotide, and coenzyme II is a triphosphopyridine nucleotide. In nicotinic acid deficiency it is possible to demonstrate a decreased cozymase content of the liver and muscle tissue. There has been some question about the cozymase content of the blood during deficiency, but all workers [34] are now agreed that the change, if demonstrable, is very slight. It is thus impossible to use this method in the diagnosis of nicotinic acid deficiency.

The dog was used as the experimental animal in all of the early work on the antipellagra vitamin. Blacktongue in the dog was first described by Chittenden and Underhill, and in 1922 Goldberger and his co-workers concluded that blacktongue in dogs was analogous to pellagra in human beings. Through the use of highly purified rations supplemented with the newer B vitamins, it has been possible to demonstrate that the growing chick needs a dietary source of nicotinic acid for optimum growth and for the prevention of chick blacktongue.[35] In the rat niacin is an essential nutrient only when the tryptophan content of the diet is low.[36] The high incidence of pellagra, when the diet contains much corn, is undoubtedly due not only to the low amount of niacin in corn but to the fact that the main protein in corn, zein, is very low in tryptophan. A definite relationship between the niacin requirement and the protein part of the diet has been demonstrated in several different species, and it is apparent that the conversion of tryptophan to niacin is the most limited in the dog. An increased excretion of N′-methylnicotinamide on administration of tryptophan has been observed in rats [37] and in human beings.[38]

The early symptoms of pellagra are weakness, lassitude, anorexia and indigestion, followed by sore and ulcerated mouth and diarrhea. The typical dermatitis usually simplifies the diagnosis. A more detailed summary of the symptoms has been made by Harris [39] and by Youmans.[40] Spies, Walker and Woods [41] have shown that infants and children also suffer from nicotinic acid deficiency in areas where pellagra is endemic, although typical lesions are seldom seen in early infancy. Nicotinic acid is now widely used in the treatment of pellagra, but its use is most successful in conjunction with other vitamins and specific natural foods.

The activity of various compounds related in structure to nicotinic acid was investigated by Woolley and his co-workers,[42] and it was concluded that only those

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compounds which may undergo oxidation or hydrolytic conversion to nicotinic acid are active in the dog. Since that time some activity has been observed in human beings with quinolinic acid, pyrazine 2,3-dicarboxylic acid and pyrazine monocarboxylic acid. A paper by Dann, Kohn and Handler [43] summarized much of the work on these compounds, and from their results, as well as results in this laboratory, one may conclude that the activity of these compounds is greatly inferior to that of nicotinic acid.

Since nicotinic acid is not required by the rat unless there is an amino acid imbalance in the diet, the dog originally used by Goldberger and his co-workers for the assay of the antipellagra potency of foods is the only animal that has been used with any success. Fairly accurate values can be obtained by comparing the growth response obtained by feeding a definite weight of food with that obtained after giving a standard dose of nicotinic acid.[44] Chemical methods may be used on many foods, and an improved method has been described by Dann and Handler.[45] The most widely used method is the microbiologic method of Snell and Wright,[46] and this method gives reliable results when proper precautions are taken for the release of the vitamin in certain foods. The best sources of nicotinic acid include liver, yeast, lean meats and, to a lesser extent, peanuts, potatoes and vegetables.

It is difficult to establish an exact figure for the nicotinic acid requirement of human beings. Balance experiments are complicated by the fact that excess nicotinic acid ingested is excreted in several different forms. N'-methyl nicotinamide is the product which has received most attention.[47] Even when human subjects are given large doses of niacin, never more than 30 to 40 per cent of the dose can be accounted for.[48]

However, Knox and Grossman [49] have identified the corresponding 6-pyridone, which is an oxidation product, and this may account for much of the remainder. The niacin requirement is not only dependent on the dietary tryptophan but part of the niacin requirement may be satisfied through bacterial synthesis in the digestive tract (Ellinger and Benesch [50]). The Food and Nutrition Board has suggested 12 to 18 mg. as the daily allowance for an adult man, and the minimum requirement has been set at 10 mg. per day.

One may readily ascertain from table 1 why pellagra will develop with diets containing high percentage of corn meal and patent flour. These materials contain 1 to 1.5 mg. per 100 Gm., and one would have to consume 1,000 Gm. to meet the minimum requirement, which, of course, is impossible. In contrast to corn, wheat contains 5 to 7 mg. per 100 Gm. and would be a reliable source of nicotinic acid if 80 to 90 per cent were not removed during the milling process.[51] Whole oats are also low in nicotinic acid but barley is somewhat higher. One serving of liver will supply the daily allowance, and one serving of lean meat will supply over half of the daily requirement. Since nicotinic acid is a very stable compound, there is little destruction during cooking and the loss is negligible unless the cooking water is discarded. Although milk and eggs are low in niacin, these foods are important in the prevention of pellagra because they carry a good supply of tryptophan. Certain compounds may function as antagonists to niacin, for example, 3-acetyl pyridine, but these compounds apparently do not occur in nature in sufficient concentration to affect the niacin requirement.

VITAMIN B_6

The term "vitamin B_6" was first applied by György to a substance present in yeast which was active in the prevention and cure of a specific type of acrodynia in rats. A specific compound was subsequently isolated in pure form almost simultaneously (1938) in five different laboratories, and it was synthesized the following year by Harris and Folkers.[52] Pyridoxine hydrochloride is a white crystalline powder, slightly bitter in taste and odorless, and possesses the empiric formula $C_8H_{12}O_3NCl$.

In 1944 it was shown [53] that two derivatives of pyridoxine, namely, pyridoxal and pyridoxamine, were more active than the original compound for the growth of certain lactic acid bacteria. The three compounds have the structural formula shown in figure 4.

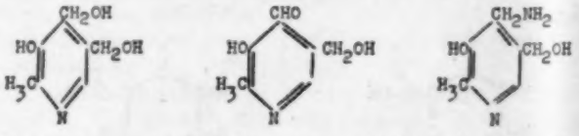

Fig. 4.—Structural formula (from left to right): pyridoxine, pyridoxal and pyridoxamine.

All three compounds are highly active in curing vitamin B_6 deficiencies in animals. All three forms occur in natural materials, although many tissues, particularly animal tissues, and yeast contain predominantly pyridoxal and pyridoxamine. Phosphorylated pyridoxal functions as a coenzyme for those enzymes which decarboxylate tyrosine, arginine, glutanic acid, "dopa," the precursor of melanin, and possibly other amino acids.[54] It also functions in reactions involving transamination [55] and tissues from pyridoxine deficient rats show a reduced amount of transaminase.[56] Pyridoxine is also closely related to tryptophan metabolism, since Lepkovsky and Nielsen [57] observed abnormal pigment in the urine of pyridoxine-deficient rats, and this was later identified as xanthurenic acid. Umbreit,

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57. Lepkovsky, S., and Nielsen, E.: A Green Pigment-Producing Compound in Urine of Pyridoxine-Deficient Rats, J. Biol. Chem. **144**: 135 (June) 1942.

Wood and Gunsalus [58] have shown that pyridoxal phosphate functions in the formation of tryptophan from indole and serine. There also appears to be a functional relation between unsaturated fatty acids and the vitamin.[59]

Pyridoxine has been shown to be essential in the nutrition of the rat,[60] the chick,[61] the dog [62] and the pig.[63] An acrodynia-like syndrome, characterized by edema, swelling and denuding of the paws and areas around the mouth and frequent thickening of the ears, is associated with pyridoxine deficiency in the rat,[64] although it has been demonstrated [65] that a lack of this vitamin may cause retarded growth without the dermatitis. The microcytic hypochromic anemia in dogs resulting from pyridoxine deficiency, reported by Fouts and his co-workers,[62] has been amply confirmed.[66]

No clearcut symptoms resulting from pyridoxine deficiency have been described in human beings. Spies, Bean and Ashe [67] have reported an additional improvement in pellagrins with pyridoxine therapy after treatment with nicotinic acid, riboflavin and thiamine. Smith and Martin [68] observed a rapid and satisfactory healing of the typical lesions of cheilitis with vitamin B_6 therapy. Although clinical treatment of such conditions as Parkinson's disease, muscular dystrophy and paralysis agitans has been studied, the results are not definite enough to permit postulation of the action of the vitamin or to associate any one of these syndromes with specific lack of pyridoxine in the diet. The human requirement is unknown, but animal experiments indicate that the vitamin B_6 requirement may be about the same as for thiamine, namely, about 1.5 mg. a day.

The most reliable method for determining the B_6 content of foods is probably the rat assay method,[65] although microbiologic methods involving Saccharomyces carlsbergensis and neurospora give values that are in reasonably good agreement with those obtained by rat assay.[69] Among the best sources are rice, bran, liver, yeast, cereals, legumes and milk. Whole wheat contains about 0.4 mg. in 100 Gm., most meats 0.4 to 0.8 mg. in 100 Gm. when fresh,[70] fresh vegetables about 0.2 mg. in 100 Gm. and milk about 1 mg. per quart (liter). Swaminathan [71] found diets consumed in India to supply 3.5 to 5 mg. a day.

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PANTOTHENIC ACID

The member of the B complex which prevented dermatitis in chicks was first called the "filtrate factor." Although the so-called filtrate fractions prepared from liver extract were effective in the prevention of black-tongue in dogs, pellagra in human beings and dermatitis in chicks, it was demonstrated as soon as nicotinic acid was accepted as the antipellagra factor that the activity of these fractions in the prevention of chick dermatitis was not due to the nicotinic acid present but to a separate and distinct vitamin. Shortly thereafter, Woolley, Waisman and I [72] and Jukes [73] independently demonstrated that pantothenic acid, which Williams and his co-workers [74] had shown to be a growth factor for yeast as early as 1933, was similar to the chick antidermatitis factor. The complete synthesis of pantothenic acid was achieved in 1940.[75] The vitamin is now available as the dextrorotatory calcium salt, which occurs in fine dense white crystals that are odorless and slightly bitter in taste. The empiric formula is $(C_9H_{16}NO_5)_2Ca$. The structural formula for the free acid is shown in figure 5.

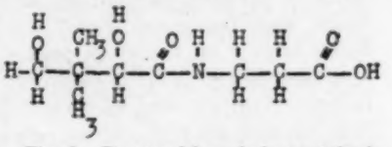

Fig. 5.—Structural formula for pantothenic acid.

Pantothenic acid is fairly stable when subjected to moist heat, especially at a neutral p_H, but is destroyed by prolonged dry heat. The compound is readily hydrolyzed into the two component parts in alkaline solution. The compound is widely distributed in nature, and recent work has shown that much of the vitamin may be present in bound forms. Lipmann and his co-workers [76] have shown that pantothenic acid is related to enzymatic acetylation. It was first shown [77] that a coenzyme was present in liver preparations which was necessary for the acetylation of aromatic amines. Later it was found [78] that the same coenzyme was needed for the acetylation of choline in brain tissue. This coenzyme was prepared in concentrated form and observed to contain about 10 per cent pantothenic acid. If pantothenic acid is related to all the biologic acetylations, it has a very important function. Riggs and Hegsted [79] have recently shown that acetylation of intraperitoneally administered p-aminobenzoic acid in rats was definitely reduced when the animals were given a diet deficient in pantothenic acid. The addition of the vitamin corrected the abnormality.

Rats placed on diets low in pantothenic acid grow very poorly, and in a few weeks necrosis of the adrenal cortex develops, which was first described by Daft and Sebrell.[80] Changes in hair pigmentation (graying)

72. Woolley, D. W.; Waisman, H. A., and Elvehjem, C. A.: Nature and Partial Synthesis of the Chick Antidermatitis Factor, J. Am. Chem. Soc. **61**: 977 (April) 1939.
73. Jukes, T. H.: Pantothenic Acid and the Filtrate (Chick Antidermatitis) Factor, J. Am. Chem. Soc. **61**: 975 (April) 1939.
74. Williams, R. J.; Lyman, C. M.; Goodyear, G. H.; Truesdail, J. H., and Haladay, D.: "Pantothenic Acid," a Growth Determinant of Universal Biological Occurrence, J. Am. Chem. Soc. **55**: 2912 (July) 1933.
75. Stiller, E. T.; Harris, S. A.; Finkelstein, J.; Keresztesy, J. C., and Folkers, K.: Pantothenic Acid: VIII. The Total Synthesis of Pure Pantothenic Acid, J. Am. Chem. Soc. **62**: 1785 (July) 1940.
76. Lipmann, F.; Kaplan, N. O.; Novelli, G. D.; Tuttle, L. C., and Guirard, B. M.: Coenzyme for Acetylation, a Pantothenic Acid Derivative, J. Biol. Chem. **167**: 869 (March) 1947.
77. Lipmann, F.: Acetylation of Sulfanilamide by Liver Homogenates and Extracts, J. Biol. Chem. **160**: 173 (Sept.) 1945.
78. Lipmann, F., and Kaplan, N. O.: A Common Factor in the Enzymatic Acetylation of Sulfanilamide and of Choline, J. Biol. Chem. **162**: 743 (March) 1946.
79. Riggs, T. R., and Hegsted, D. M.: Effect of Pantothenic Acid Deficiency on Acetylation in Rats, J. Biol. Chem. **172**: 539 (Feb.) 1948.
80. Daft and Sebrell, cited by Daft, F. S.; Sebrell, W. H.; Babcock, S. H., Jr., and Jukes, T. H.: Effect of Synthetic Pantothenic Acid on Adrenal Hemorrhage, Atrophy and Necrosis in Rats, Pub. Health Rep. **55**: 1333 (July 26) 1940.

have been observed in many laboratories when black or piebald rats were used. Unna, Richards and Sampson [81] have published reproductions of photographs illustrating these fur changes in nutritional achromotrichia. Schaefer, McKibbin and I [82] have produced acute deficiencies of pantothenic acid in dogs that are characterized by sudden collapse associated with decreased blood dextrose, increased nonprotein nitrogen and lowered levels of blood chlorides. Severe intussusception in the intestinal tract and fatty livers have also been observed. Phillips and Engel [83] have reported specific neuropathologic changes of the spinal cord in chicks suffering from deficiency of pantothenic acid. Wintrobe, Miller and Lisco [84] have also observed neuropathologic changes in pigs on synthetic diets low in pantothenic acid and other members of the B complex.

In spite of these interesting symptoms in experimental animals, little is known about the real significance of pantothenic acid in nutrition of human beings. Spies and his co-workers [85] concluded from studies based largely on values of pantothenic acid in the blood that pantothenic acid is essential to nutrition of human beings. Krahnke and Gordon [86] have studied the excretion of pantothenic acid in persons on different levels of intake. However, no specific symptoms in human beings have been correlated with a deficiency of the vitamin. This may be due to the fact that pantothenic acid is widely distributed and that even restricted diets may not be low enough to cause a serious deficiency.

No figures can be given for the daily human requirement. The relatively high amount of pantothenic acid needed to produce good growth in rats on synthetic diets has led to the assumption that the requirement is considerably higher than that of some of the other B vitamins. However, work in this laboratory indicates that the requirement for dogs can be satisfied with 0.10 mg. per hundred grams ration, a level similar to that of thiamine and riboflavin. According to these results, the human requirement cannot be above 5 mg. a day.

The pantothenic acid content of foods may be measured by growth experiments with chicks, but the microbiologic methods [87] are now in more general use. However, in order to obtain the total pantothenic acid in foods when microbiologic methods are used, it is necessary to treat the material with a liver enzyme and an intestinal phosphatase.[88] Liver is one of the richest natural sources, but meats, cereals and milk are also reliable sources. A few studies [89] have been made on the loss of pantothenic acid during cooking; there is, as one would expect, some loss, the retention varying from 60 to 100 per cent. Evidence is available to show that only about one half of the pantothenic acid in whole wheat is lost during the milling process.

81. Unna, K.; Richards, G. V., and Sampson, W. L.: Studies on Nutritional Achromotrichia in Rats, J. Nutrition **22**: 553 (Dec.) 1941.
82. Schaefer, A. E.; McKibbin, J. M., and Elvehjem, C. A.: Pantothenic Acid Deficiency Studies in Dogs, J. Biol. Chem. **143**: 321 (April) 1942.
83. Phillips, P. H., and Engel, R. W.: Some Histopathologic Observations on Chicks Deficient in the Chick Antidermatitis Factor or Pantothenic Acid, J. Nutrition **18**: 227 (Sept.) 1939.
84. Wintrobe, M. M.; Miller, J. L., Jr., and Lisco, H.: The Relation of Diet to the Occurrence of Ataxia and Degeneration of the Nervous System of Pigs, Bull. Johns Hopkins Hosp. **67**: 377 (Dec.) 1940.
85. Spies, T. D.; Stanbery, S. R.; Williams, R. J.; Jukes, T. H., and Babcock, S. H., Jr.: Pantothenic Acid in Human Nutrition, J. A. M. A. **115**: 523 (Aug. 17) 1940.
86. Krahnke, H. F., and Gordon, E. S.: Pantothenic Acid in Human Nutrition, J. Clin. Investigation, to be published.
87. Pennington, D.; Snell, E. E., and Williams, R. J.: An Assay Method for Pantothenic Acid, J. Biol. Chem. **135**: 213 (Aug.) 1940. Pelzar, M. J., Jr., and Porter, J. R.: A Microbiological Assay Technic for Pantothenic Acid with the Use of Proteus Morganii, ibid. **139**: 111 (May) 1941. Strong, F. M.; Feeney, R. E., and Earle, A.: Microbiological Assay for Pantothenic Acid, Indust. & Engin. Chem. (Anal. Ed.) **13**: 566 (Aug.) 1941. Jukes, T. H.: The Biological and Microbiological Assay of Pantothenic Acid, Biol. Symposia **12**: 253, 1947.
88. Neilands, J. B., and Strong, F. M.: The Enzymatic Liberation of Pantothenic Acid, Arch. Biochem., to be published.
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CHOLINE

Choline is a colorless viscous fluid, and the more familiar choline chloride is a very hygroscopic white crystalline substance, with a salty bitter taste. The formula for choline is shown in figure 6. As expected from its chemical constitution, the compound is not stable to alkali treatment, but is stable to acids even at elevated temperatures.

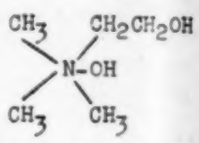

Fig. 6.—Structural formula for choline.

Choline has been recognized for many years as a component part of the phospholipid lecithin, but its functional importance in nutrition was not apparent until Best demonstrated its role in the prevention of fatty livers in depancreatized dogs.[90] Choline is now considered an important member of the B complex, because most experimental animals, when placed on diets low in this compound and its precursors, show characteristic symptoms. The most obvious changes include the development of fatty livers and hemorrhagic renal lesions. The high requirement of the young rat for choline has been stressed by Griffith,[91] who reported fatty degeneration of the liver, renal lesions, ocular hemorrhages and regression of the thymus within ten days after the rats had been placed on a choline-low, but otherwise adequate, diet. When the deficiency persists in animals which have fatty deposits in the liver, cirrhosis will develop. In the early stages, this secondary change is also reversible if adequate choline is added to the diet.

The function of choline must therefore be related to the mobilization of fatty acids in the body. Experiments with the dog and the rat have demonstrated that neutral fat is involved, since fatty livers induced by feeding high cholesterol diets do not respond to choline therapy. The observations of du Vigneaud and his collaborators [92] that the methyl groups of choline, as well as those of methionine and betaine, are transferable in the animal organism has led to the postulation that one of the functions of choline is to supply labile methyl groups. McHenry [90] stated that there is evidence now that choline may function in at least three ways: to stimulate the formation of phospholipids, to make possible the production of acetyl choline or to supply labile methyl groups.

Extensive reviews have been published on choline and the reactions involved in biologic transmethylation by Best and Lucas,[93] Jukes [94] and du Vigneaud.[95]

90. McHenry, E. W.: Choline, the B Vitamins and Fat Metabolism, Biol. Symposia **5**: 177, 1941.
91. Griffith, W. H.: The Nutritional Importance of Choline, J. Nutrition **22**: 239 (Sept.) 1941.
92. du Vigneaud, V.; Chandler, J. P.; Moyer, A. W., and Keppel, D. M.: The Effect of Choline on the Ability of Homocystine to Replace Methionine in the Diet, J. Biol. Chem. **131**: 57 (Nov.) 1939. du Vigneaud, V.: The Interrelationship Between Choline and Other Methylated Compounds, Biol. Symposia **5**: 234, 1941.
93. Best, C. H., and Lucas, C. C.: Choline—Chemistry and Significance as a Dietary Factor, in Harris, R. S., and Thimann, V. K.: Vitamins and Hormones: Advances in Research and Applications, New York, Academic Press, Inc., 1943, vol. 1, p. 1.
94. Jukes, T. H.: Choline, Ann. Rev. Biochem. **16**: 193, 1947.
95. du Vigneaud, V.: The Significance of Labile Methyl Groups in the Diet and Their Relation to Transmethylation, in Harvey Lectures, 1942-1943, Baltimore, Williams & Wilkins Company, 1943, p. 39.

Jukes [96] has shown that choline is one of the factors required in addition to adequate manganese to prevent slipped tendon in young turkeys. Sure [97] reported that choline is indispensable for lactation in adult rats and in the prevention of paralysis in suckling rats. Depression of the growth rate when choline is omitted from the diet has been observed in the case of the rat by Richardson, Hogan, Long and Itschner,[98] in the chick by Hegsted, Mills, Hart and me [99] and in the dog by Schaefer, McKibbin and me.[100]

The choline requirement, even for the rat, is difficult to establish, since the amount depends on the methionine and betaine content of the ration. Most of the synthetic rations which are now used for experimental work contain 100 mg. of choline in 100 Gm. From this figure one might suggest that the human requirement would be less than 500 mg. a day. It has been estimated that the choline intake from an average human diet may range from 250 to 600 mg. The problem of estimating accurately the choline content of food materials is also a difficult one, since most salts of choline are very soluble in water except a few, like the periodide and the reineckate, which have been used in quantitative estimations. The most specific methods for determining choline are the estimation of acetyl choline after acetylation and the use of the microbiologic assay involving the cholineless mutant (no. 34486) of Neurospora crassa. These methods have been reviewed by Handler.[101]

By far the best dietary source of choline is egg yolk, while soybean meal, liver, dried yeast, pancreas, brain and kidney are good sources. Most edible fats are very low in choline. It should be pointed out that free choline is rarely found in food materials and is present mainly as complex phosphoric acid esters. Most diets contain sufficient choline and its precursors to meet the ordinary needs. However, evidence is accumulating that some types of clinical cirrhosis are favorably affected by dietary treatment including choline and other vitamins, together with a high protein diet.

BIOTIN

Biotin was first recognized as a growth factor for yeast and was isolated by Kögl and Tonnis [102] in 1936. In 1940 du Vigneaud and his co-workers [103] demonstrated that biotin, the yeast growth factor, was the same as the anti-egg white injury factor, or vitamin H, in animal nutrition. György had carried out extensive studies on the properties of vitamin H, and, after it was shown that biotin was identical with this factor, du Vigneaud, Hofmann, Melville and György [104] described the isolation of biotin from liver. The structure was studied by du Vigneaud and co-workers,[105] and its synthesis was announced by Harris and his co-workers [106] in 1943. Free biotin has the structure shown in figure 7. It is a very stable compound, resisting autoclaving with strong mineral acids and in the form found in natural products is but slowly inactivated by alkali. The pure biotin, however, shows appreciable lability to alkali. Both the free and bound biotin are inactivated by oxidizing agents.

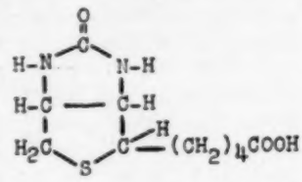

Fig. 7.—Structure of free biotin.

It has been known for many years that a characteristic syndrome can be produced in rats fed diets containing rather high amounts of raw egg white. Lease, Parsons and Kelly [107] observed that the rabbit and the monkey also exhibited a characteristic dermatitis when fed rations rich in egg white. As early as 1933 Parsons, Lease and Kelly [108] concluded that the injury involved an interrelation between a positive toxicity and a relative absence of a protective factor.

György, Rose, Eakin, Snell and Williams [109] have established the presence of "avidin" (an albumin) as the biotin-inactivating factor in egg white. Thus, it becomes apparent that egg white injury is due to the unavailability of biotin by virtue of being tied up with avidin, in which complex biotin cannot be absorbed from the intestine and is excreted in the feces. Nielsen and I,[110] using a more complete ration than had been used in the early work, were able to demonstrate a biotin deficiency in the rat fed 10 per cent levels of egg white. Typical symptoms of "spectacled eye" progressing to general alopecia and, in the later stages, the onset of a spasticity and final death of the animal were recorded. Even the severe symptoms of spasticity were cured when excess biotin (in excess of that which unites with the avidin) was added to the diet. With the synthetic diet without the egg white, these workers were unable to demonstrate any signs of biotin deficiency, and it seems probable that under most conditions the rat can synthesize, through the medium of bacteria in the intestine, sufficient biotin for its requirement. Biotin deficiency has been reported in the chick without resort to egg white diets, which seems to indicate that very limited synthesis of biotin in the intestinal tract must prevail. A typical dermatitis, involving the feet, was observed by Hegsted and his co-workers [111] to be characteristic of the deficiency in the chick, and Patrick and his co-workers [112] also noted similar dermatitis with turkeys on biotin-deficient rations. Waisman, McCall and I [113] described the production

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97. Sure, B.: The Essential Nature of Choline for Lactation and Growth of the Albino Rat, J. Nutrition **19**: 71 (Jan.) 1940.

98. Richardson, L. R.; Hogan, A. G.; Long, B., and Itschner, K. L.: The Number of Vitamins Required by the Rat, Proc. Soc. Exper. Biol. & Med. **46**: 530 (April) 1941.

99. Hegsted, D. M.; Mills, R. C.; Elvehjem, C. A., and Hart, E. B.: Choline in the Nutrition of Chicks, J. Biol. Chem. **138**: 459 (April) 1941.

100. Schaefer, A. E.; McKibbin, J .M., and Elvehjem, C. A.: Importance of Choline in Synthetic Rations for Dogs, Proc. Soc. Exper. Biol. & Med. **47**: 365 (June) 1941.

101. Handler, P.: The Determination of Choline in Biological Material, Biol. Symposia **12**: 361, 1947.

102. Kögl, F., and Tonnis, B.: Plant Growth Substances: XX. The Bios Problem; Isolation of Crystalline Biotin from Egg Yolk, Ztschr. f. physiol. Chem. **242**: 43 (Aug.) 1936.

103. du Vigneaud, V.; Melville, D. B.; György, P., and Rose, C. S.: On the Identity of Vitamin H with Biotin, Science **92**: 62 (July 19) 1940.

104. du Vigneaud, V.; Hofmann, K.; Melville, D. B., and György, P.: Isolation of Biotin (Vitamin H) from Liver, J. Biol. Chem. **140**: 643 (Aug.) 1941.

105. du Vigneaud, V.; Hofmann, K., and Melville, D. B.: On the Structure of Biotin, J. Am. Chem. Soc. **64**: 188 (Jan.) 1942.

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107. Lease, J. G.; Parsons, H. T., and Kelly, E.: A Comparison in Five Types of Animals of the Effects of Dietary Egg White and of a Specific Factor Given Orally or Parenterally, Biochem. J. **31**: 433 (March) 1937.

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109. György, P.; Rose, C. S.; Eakin, R. E.; Snell, E. E., and Williams, R. J.: Egg White Injury as the Result of Nonabsorption in Inactivation of Biotin, Science **93**: 477 (May 16) 1941.

110. Nielsen, E., and Elvehjem, C. A.: Cure of Spectacle Eye Condition in Rats with Biotin Concentrates, Proc. Soc. Exper. Biol. & Med. **48**: 349 (Oct.) 1941.

111. Hegsted, D. M.; Oleson, J. J.; Mills, R. C.; Elvehjem, C. A., and Hart, E. B.: Studies on a Dermatitis in Chicks Distinct from Pantothenic Acid Deficiency, J. Nutrition **20**: 599 (Dec.) 1940.

112. Patrick, H.; Boucher, R. V.; Dutcher, R. A., and Knandel, H. C.: Biotin and Prevention of Dermatitis in Turkey Poults, Proc. Soc. Exper. Biol. & Med. **48**: 456 (Nov.) 1941.

113. Waisman, H. A.; McCall, K. B., and Elvehjem, C. A.: Acute and Chronic Biotin Deficiencies in the Monkey, J. Nutrition **29**: 1 (Jan.) 1945.

of chronic biotin deficiency in the monkey with biotin-deficient diets and acute biotin deficiency through the use of egg white.

Recent work has established a more definite role for biotin in metabolism. It apparently functions in the carboxylation of pyruvate to yield oxalacetate. Working with Lactobacillus arabinosus, Shive and his co-workers [114] and Lardy and his associates [115] have shown that either oxalacetate or aspartate can partially replace biotin in the growth of this organism. Another function of biotin can be replaced by oleic acid, and Potter and I [116] have shown that when both aspartic acid and oleic acid are present good growth can be obtained in the absence of biotin.

While rather definite requirements can be established for chicks, the requirement for many animals, including man, is difficult to establish, since a large part may be supplied by the intestinal bacteria. Oppel [117] showed that the urinary excretion of biotin in human subjects exceeded that in the diet and in all cases the biotin content of the feces was considerably higher. Sydenstricker and his co-workers [118] reported that dermatitis and changes in the color of the skin which responded to biotin were produced in human subjects by feeding diets with high levels of egg white. Some have experienced difficulty in repeating these observations, but the variations may depend on the degree of intestinal synthesis. In any case, there seems to be no difficulty in supplying an adequate amount of biotin in human beings on average diets.

Biotin can be conveniently determined by use of microbiologic methods of assay in which responses in yeast growth (Snell, Eakin and Williams [119]) or acid production by Lactobacillus casei (Shull, Hutchings and Peterson [120]) are measured. Biotin is rather ubiquitous in distribution, but liver, kidney, yeast and egg yolk are the chief sources. It is to be emphasized that in most tissues biotin is present in a "bound" state, in which it cannot be extracted by hot water, and autolysis or acid hydrolysis must be employed to realize the true concentration of biotin in these instances. Wright [121] summarized methods for the microbiologic determination of biotin as well as the compounds which inhibit the response of microorganisms to biotin.

INOSITOL

Inositol is a crystalline substance with a sweet taste and is a hexahydroxycyclohexane comparable to the cyclic form of glucose. The biologically active form of inositol is one of the optically inactive forms known as i-inositol or meso-inositol, with the stereochemical structure shown in figure 8.

It is a very stable compound, resisting strong acid and alkali treatment. It is found in plants, where it occurs in free form and as "phytin," a calcium magnesium salt of inositol phosphoric acid. In the animal body inositol is found in muscle (accounting for the term "muscle sugar"), brain, blood erythrocytes and eye tissues and as phytin in the red blood cells of chickens and turtles. It also occurs in lipositol, which is a complex containing inositol monophosphate linked to galactose and combined with ethanolamine, tartaric acid, oleic acid and various saturated fatty acids. Aside from its presence in biologic matter in the various forms, little is known about its specific function.

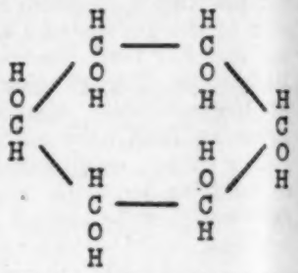

Fig. 8.—Structure of inositol.

The relation of inositol to the nutrition of animals was first indicated by the report of Woolley,[122] who isolated the substance from liver and showed it to be the constituent factor responsible for the cure of mouse alopecia. Later Pavcek and Baum [123] were able to demonstrate a growth response and a cure of spectacled eye in rats. The curative action and growth effect of inositol seems to be related to the amount and type of fat in the diet, since the syndrome was produced on fat-free or low butter fat rations and not on those containing 14 per cent "crisco." A recent report by Lindley and Cunha,[124] who worked with swine, indicates a possible interrelationship between inositol and biotin, and this may explain why inositol was active in the prevention of the spectacled eye condition in rats. Sure [125] has presented data which indicate that inositol may be required by the lactating rat. Martin, Thompson and de Carvajal-Forero [126] have injected rather low levels (10 mg. per kilogram of body weight) of inositol into dogs and observed intestinal motility to be greatly increased. A definite growth increment in the chick was obtained by feeding inositol in conjunction with a synthetic ration.[127] In the rat, inositol was observed to have an effect similar to lipocaic in preventing the fatty livers produced by the feeding of liver fractions or purified biotin preparations.[128]

Inositol can be determined in tissues and foods by using a microbiologic assay employing a specific strain of yeast as the test organism.[129] By this method of determination, Williams and his co-workers [130] have run large numbers of assays on various rat and beef tissues and observed spleen, heart, kidney, brain, thyroid and testes to be especially high in inositol content.

The requirements for inositol are not known. Deficiency symptoms in mice have been cured by feeding 10 mg. of inositol in 100 Gm. of food. Most purified

114. Shive, W., and Rogers, L. L.: Involvement of Biotin in the Biosynthesis of Oxalacetic and α-Ketoglutaric Acids, J. Biol. Chem. **169**: 453 (July) 1947.

115. Lardy, H. A.; Potter, R. L., and Elvehjem, C. A.: The Role of Biotin in Bicarbonate Utilization by Bacteria, J. Biol. Chem. **169**: 451 (July) 1947.

116. Potter, R. L., and Elvehjem, C. A.: Biotin and the Metabolism of Lactobacillus Arabinosus, J. Biol. Chem. **172**: 531 (Feb.) 1948.

117. Oppel, T. W.: Studies of Biotin Metabolism in Man, Am. J. M. Sc. **204**: 856 (Dec.) 1942.

118. Sydenstricker, V. P.; Singal, S. A.; Briggs, A. P.; DeVaughn, N. M., and Isbell, H.: Observations on the "Egg White Injury" in Man, J. A. M. A. **118**: 1199 (April 4) 1942.

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123. Pavcek, P. L., and Baum, H. M.: Inositol and Spectacled Eye in Rats, Science **93**: 502 (May 23) 1941.

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125. Sure, B.: Dietary Requirements for Fertility and Lactation: XXX. Role of *p*-Aminobenzoic Acid and Inositol in Lactation, Science **94**: 167 (Aug. 15) 1941.

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127. Hegsted, D. M.; Briggs, G. M., Jr.; Mills, R. C.; Elvehjem, C. A., and Hart, E. B.: Inositol in Chick Nutrition, Proc. Soc. Exper. Biol. & Med. **47**: 376 (Jan.) 1941.

128. Gavin, G., and McHenry, E. W.: Inositol: A Lipotropic Factor, J. Biol. Chem. **139**: 485 (May) 1941.

129. Woolley, D. W.: A Method for the Estimation of Inositol, J. Biol. Chem. **140**: 453 (Aug.) 1941.

130. Williams, R. J.; King, A.; Mitchell, H. K., and McMahan, J. R.: Assay Method for Inositol: Studies on the Vitamin Content of Tissues: I, Publication 4137, Austin, Texas, University of Texas Press, 1941, p. 27.

rations which are now used for experimental purposes contain this level of inositol.

Little is known regarding the role of inositol in human nutrition. Perhaps the most interesting development is the report of Milhorat and Bartels [131] that inositol may improve the action of tocopherol in the treatment of progressive muscle dystrophy. These authors suggested that inositol forms a complex with tocopherol in the intestinal tract and that this complex is necessary for normal creatine metabolism.

PARA-AMINOBENZOIC ACID

Another factor which is often included in the B complex is para-aminobenzoic acid (fig. 9).

Fig. 9.—Structure of para-aminobenzoic acid.

It was first recognized as an essential metabolite when Woods [132] discovered the antagonistic action between this compound and sulfanilamide and the consequent identification of para-aminobenzoic acid as a bacterial growth factor.[133] The relation of sulfonamide drugs and para-aminobenzoic acid has been reviewed by Welch.[134] The report by Ansbacher [135] that the graying of the fur observed in rats on certain synthetic rations could be cured by the administration of 3 mg. of para-aminobenzoic acid daily stimulated much interest in this compound as an animal factor. Numerous papers have appeared dealing with this compound as it affects hair color, growth and lactation in rats and other animals, but most of the results are conflicting. Briggs and his co-workers [136] observed a growth response on adding para-aminobenzoic acid to purified rations for chicks, but suggested that it acts indirectly by stimulating the production of unknown vitamins through intestinal synthesis. The possible role of para-aminobenzoic acid in the treatment of gray hair in human beings has been studied by Brandaleone and his associates,[137] who reported that in a group of 19 elderly persons with gray hair only 2 persons showed a significant color change during a period of intensive vitamin therapy. At present there appears to be no clearcut evidence that this metabolite must be supplied preformed in the diet of human beings. The contradictory results which have been obtained may be due to the fact that this compound is a constituent of the folic acid molecule.

The most striking observation regarding para-aminobenzoic acid is its chemotherapeutic effect on typhus [138] and Rocky Mountain spotted fever.[139]

FOLIC ACID

Chemically, folic acid is N-[4-{[2-amino-4-hydroxy-6-pteridyl)methyl]amino}benzoyl] glutamic acid, or pteroyl glutamic acid.[140] It is a yellow compound sparingly soluble in water and has the structure shown in figure 10. This molecule contains three different

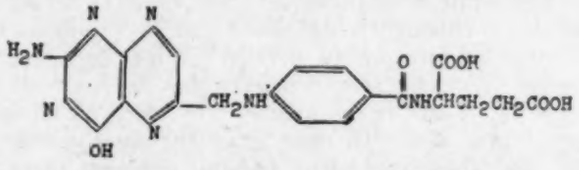

Fig. 10.—Structure of folic acid (pteroyl glutamic acid).

groups: the pteridine part, para-aminobenzoic acid and glutamic acid. The part consisting of the pteridine and para-aminobenzoic acid is called pteroic acid.

Folic acid is widely distributed in nature, both in free form and in compounds with added glutamic acid, such as pteroyl triglutamic acid (fermentation factor) and pteroyl heptaglutamate (vitamin B_c conjugate).[141]

In light of our present knowledge, it is apparent that folic acid deficiencies were observed over ten years ago in monkeys (Day and his co-workers [142]) and in chicks (Hogan and Parrott [143]). Greatest progress in the isolation of this vitamin was made when it was recognized that a growth factor was needed for the growth of Lactobacillus casei and related organisms [144] and that concentrates of this factor were active for growth and hemoglobin production in chicks fed purified rations.[145]

Most knowledge concerning the function of folic acid has come from studies on bacterial metabolism. Nimmo Smith and Woods [146] have shown that all organisms requiring para-aminobenzoic acid grow equally well when given folic acid, although the required molar concentration of folic acid was greater than that of para-aminobenzoic acid. Folic acid also acted as an antisulfonamide agent with these organisms, although the activity differed from that of para-aminobenzoic acid in that it was noncompetitive. Stokes [147] and Lampen and Jones [148] have suggested that folic acid functions as a prosthetic group in an enzyme concerned with the synthesis of thymine or related compounds.

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Today it is well established that synthetic folic acid is required for growth and blood formation in chicks,[149] monkeys [150] and fox and mink.[151] Rats do not require preformed folic acid in the diet until the synthesis of this compound by intestinal bacteria is reduced through the use of sulfonamide drugs.[152] Similarly, dogs grow and regenerate hemoglobin very well on diets devoid of folic acid, although a deficiency can be produced by allowing blacktongue to develop in the dog several times.[153] A folic acid deficiency has been produced in the pig [154] and in the mouse [155] by using an antagonist of folic acid. In most cases the three forms of folic acid show equivalent activity, although there is some evidence that the pteroyl heptaglutamic acid is not as active in the monkey as pteroyl glutamic acid.[156]

The human being is apparently similar to the rat and dog in that the requirement is satisfied by intestinal production except under disturbed conditions. Attempts to deplete volunteer subjects of their tissue reserves of folic acid by supplying diets adequate in other essential nutrients but low in folic acid have not been successful. In spite of this fact, the activity of synthetic folic acid in various types of macrocytic anemia in relapse has repeatedly been demonstrated. The activity of pteroyl glutamic acid was first demonstrated during the latter part of 1945 and the extensive clinical studies have been summarized by Spies and his co-workers,[156] Darby [157] and Cartwright.[158] Darby [157] has also described the effects of pteroyl glutamic acid on the gastrointestinal manifestations of sprue and related syndromes. Since commercial preparations of the classic pernicious anemia factor contain practically no folic acid [159] and since a pure substance, vitamin B_{12}, which is active in very small amounts in the treatment of pernicious anemia, has now been isolated,[160] it is clear that the effect of folic acid may not be direct or that its effect is closely related to additional factors. It is entirely possible that extensive use of vitamin B_{12} in the treatment of anemia in human beings will bring out conditions that will respond only to folic acid. Such a condition has been obtained in the dog on low protein–low niacin diets.[161]

It is difficult to suggest any figures for the folic acid requirement of human beings. Clinical responses have been obtained with 2 to 10 mg., but this intake must be considerably higher than the daily requirement. On the basis of the requirements for other animals, a figure of 0.1 to 0.2 mg. per day may be reasonable.

Microbiologic methods have been used almost exclusively for the estimation of the folic acid content of foods, although chick assays have been used for comparison. In fact, it was the discrepancy between the chick assay and the microbiologic assay which led to the isolation of the conjugate which has activity for the chick but not for bacteria.[162] In 1942 Cheldelin and Williams [163] reported the folic acid content of many foods, but at that time it was necessary to use a standard of assumed potency since the crystalline vitamin was not available. Cheldelin and his co-workers [164] found taka-diastase the most effective of several enzymes studied for the release of folic acid, but later work has shown that a water extract of fresh hog kidney, as described by Bird and his co-workers [165] gives higher results. Olson and his co-workers [166] have studied some of the difficulties encountered in the release of folic acid in liver homogenates. The results of a preliminary report [167] on the folic acid content of foods show liver and deep green leafy vegetables to be very high and green vegetables, cauliflower, kidney, muscle meat and wheat cereals to be high in folic acid values. Preliminary results also indicate that the loss of folic acid during cooking may be very high, although improved methods for the release of conjugated forms may alter the results somewhat. There is also considerable loss in vegetables during storage at room temperature.

COMMENT

So far, ten members of the B complex have been described and a pure compound has been associated with each vitamin. During the early studies on the additional factors required by the chick, Briggs and his co-workers [168] described two factors: one which showed greatest activity in the promotion of growth and one which was more active in stimulating feather production. On the basis of microbiologic assays, which did not include enzymatic treatment for the complete release of folic acid, both appeared to be different from the bacterial growth factor (folic acid), and they were designated B_{10} and B_{11}. When synthetic folic acid became available, an adequate amount added to

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synthetic rations produced excellent growth, feathering and hemoglobin production. Folic acid appears to replace the two factors, although part of the effect may be indirect. The exact relation of folic acid to vitamin B_{10} and vitamin B_{11} will have to await new technics.

VITAMIN B_{12}

Rickes and his associates [169] have isolated from liver a crystalline compound which is highly active in patients with Addisonian pernicious anemia.[169] On the basis of the aforementioned terminology, this compound has been called vitamin B_{12}. This compound is also active for the growth of Lactobacillus lactis.[170] The availability of this compound for unrestricted experimental work will do much to establish the exact relation of folic acid to macrocytic anemias.

ADDITIONAL FACTORS

The existence of several additional factors is evident from studies with a number of different animal species. In the case of rats, it has been shown that liver and liver preparations will stimulate the rate of growth of these animals when they are maintained on a corn-soybean ration [171] or fed a basal ration with added thyroid.[172] Cary and his co-workers [173] have developed an assay for an unknown factor, called factor X, by prolonged extraction of the casein used in the ration and by depleting the young by feeding their mothers a diet deficient in factor X. Commercial liver extracts were observed to contain this factor. A growth response can be obtained in chicks fed a corn-soybean ration by adding fish products [174] or preparations from cow manure.[175] Chicks maintained on a similar ration also respond to the injection of very small quantities of liver concentrates rich in the pernicious anemia factor.[176] When dogs are placed on diets deficient in niacin and folic acid and containing a sulfonamide drug, the animals finally fail to respond to the addition of these two vitamins. Highly purified liver concentrates given intramuscularly are highly effective in producing growth and hematopoietic responses.[161] Whether the same factor is concerned in all these reactions and whether vitamin B_{12} will function in any of the conditions remains to be determined.

Recent studies show that in monkeys fed highly purified rations deficient in folic acid or riboflavin a type of anemia develops which responds only when fresh liver or raw milk is given.[23] In this case liver concentrates are inactive, which indicates that the factor is separate and distinct from those previously mentioned.[177] This factor may be related to one of the two factors observed to be needed by the fox and mink for normal growth and development.[178]

The availability of the several synthetic water-soluble vitamins has been of the greatest value in clinical practice and also for the fortification of certain foods, but the common foods still remain the best source of these vitamins in practical nutrition. Aside from the gustatory significance of properly prepared natural foods, the greatest value obtained from their consumption is that they supply the unknown factors along with the known. All the known water-soluble vitamins may be obtained from natural foods through proper selection. The selection is not an easy task even with the modern methods of food production and distribution. Some of the modern methods of processing increase rather than decrease the difficulties. Often more emphasis is placed on the mere use of natural foods than on the proper combination of these foods. The few values given in table 1 clearly indicate the fallacy of this emphasis. Different natural foods differ greatly in the amount of any given vitamin which they contain. Thus, apples contain 0.04 mg. and pork loin 1.0 mg. of thiamine in 100 Gm. Eggs supply 0.1 mg. and peanuts 16 mg. of nicotinic acid in 100 Gm. In addition, any one food may show large variations in the amount of the different B vitamins present. Thus, oatmeal contains 0.65 mg. of thiamine, but only 0.14 mg. of riboflavin, in 100 Gm., while liver contains 0.27 mg. of thiamine and 2.8 mg. of riboflavin in 100 Gm.

TABLE 2.—*Vitamin Content of a Few Commercial Concentrates*

Sample	Thiamine*	Riboflavin*	Niacin*	Vitamin B_6*	Pantothenic Acid*
A	5.0	3.0	20.0	0.5	3.0
B	1.0	1.0	0.15	0.03	0.2
C	2.5	2.5	20.0	0.5	...
D	1.0	0.1	....	...	...
E	1.5	2.0	20.0	0.2	1.0
F	0.6	0.1	....	...	...
G	1.5	2.0	....	...	...
H	1.5	1.0	....	...	...
I	1.0	0.33	5.0	...	...

* Values are given in milligrams per unit of product.

There has been an increasing interest in eliminating the effect of this variation by prescribing vitamin concentrates. In other words, a tablet or a capsule may supply the daily requirement of the vitamins, and any pleasing combination of foods may be consumed for the rest of the day. A survey conducted at the time the first "Handbook of Nutrition" was prepared showed that the concentrates varied to a much greater extent than do natural foods. A resurvey of typical concentrates on the market shows that this variation has decreased to a considerable extent, but one still finds products varying from 0.6 to 5 mg. of thiamine per unit of product. Niacin values vary from 0.15 to 20 mg. These products are useful in the treatment of specific deficiencies, but unless they are properly used they give no greater security than the proper combination of natural foods. Thus, one not only needs to identify all the essential vitamins, but one must give consideration to distribution of these factors in food and food preparations as well as to the daily requirements of human beings.

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SATURDAY, NOVEMBER 27, 1948

NUTRITIONAL CONTRIBUTIONS OF WHEAT

The importance of wheat in the basic food economy of most nations of Western civilization has been obvious in recent years. Wheat and wheat flour have frequently played a strategic role in preventing or alleviating mass hunger and starvation in various parts of the world. Wheat flour is one of the least expensive sources of food. Its chief use continues to be for bread. No other single food item is so commonly used to supplement calories supplied by more expensive types of foods.

A 1 pound loaf of plain baker's bread provides about 1,200 calories; a pound of flour provides roughly 1,600 calories. In the proportions in which these food items are included in American dietaries, the slightly lower digestibilities of longer extraction types of flours and of bread made from these are of little practical importance. Half a standard loaf of bread (eight 1 ounce slices), with 1 level teaspoon or one-half an average-sized pat of butter or margarine per slice, provides approximately 900 calories.

Seventy-five to eighty-five per cent of the caloric value of flour is derived from starch. Starch also supplies 60 to 80 per cent of the caloric value of bread, depending on variations in the bread formula. The public, impressed by years of advertising of bread, flour and other grain products as "energy foods" and the association of starch with calories, is unaware that comparable weights or volumes of sugar or fats exceed the caloric values of starch, flour, bread and most other grain products. Our national diet has therefore greatly increased in both sugar and fat (butter excluded) content over the past fifty years, while consumption of flour and bread has declined.

All essential amino acids are represented in the proteins of wheat, flour and bread. The amino acids in these foods do not occur, however, in sufficient or in as well proportioned quantities, relative to human requirements, as in various other food proteins, particularly those of eggs, milk and meats.

The supplementary relationships of bread or flour to various food proteins of animal origin are an important economic factor often overlooked by physicians and nutritionists. Dietary protein derived in proportions of one half to two thirds from foods of plant origin is entirely adequate in quality to meet all protein needs for normal growth, development, reproduction and lactation. As foods of plant origin are usually cheaper than foods of animal origin, the economic benefits of such mixtures are obvious.

The commendable practice of adding 6 per cent dry milk solids to the baker's mix adds a small, but definite, quantity of supplementary animal protein. This practice also adds other important nutrients; namely, calcium and riboflavin. In animal-feeding experiments,[1] the feeding of bread containing 6 per cent nonfat milk solids resulted in improved growth-promoting and bone-calcifying values as well as increased hemoglobin production. Investigators found that "enriched white bread with skim milk solids is the equal of whole-wheat bread in the production of growth and in the production of blood hemoglobin and is distinctly superior to it in the production of bone calcification."

Half a standard loaf of baker's bread provides about 18 Gm. of protein or approximately 30 per cent of the usually recommended need for protein maintenance of normal human adults other than pregnant and lactating women.

The Council on Foods and Nutrition of the American Medical Association as early as 1939 recommended that iron and certain vitamins normally present in wheat but largely removed in the milling of white flour be restored to the flour. This recommendation was made because flour and bread were almost universally consumed by the populace and were especially prominent articles of diet among low income groups whose diets were most in need of improvement in protective food values. Also, many diets might be relatively low in one or more of the essential nutrients now included as enrichment ingredients of white flour and bread. Now approximately 75 to 80 per cent of all white flour and bread is being enriched with thiamine, riboflavin, nicotinic acid and iron according to standards promulgated for enrichment of these products under authority of the Food, Drug and Cosmetic Act. Twenty-three states and two territories to date have enacted laws requiring the enrichment of all family white flour and all baker's white bread. Full scale enrichment would result in an increase of 30 to 40 per cent in the apparent per capita consumption of these three B-vitamins and iron. The enrichment program is of great benefit to the American diet and is of greatest benefit to those whose consumption of bread is highest. These in general are the persons and families with moderate to low incomes.

1. Mitchell, H. H.; Hamilton, T. S., and Shields, J. B.: J. Nutrition 25: 585, 1943.

Apparent per capita consumption of flour in this country declined from about 210 pounds (about 95.2 Kg.) per annum forty years ago to about 155 to 157 pounds (70.3 to 71.2 Kg.) per annum in the years immediately preceding World War II. Consumption increased during the war years, at which time the level was undoubtedly affected by shortages of other foods.

The long and more or less persistent decline in per capita consumption of flour is believed by many to stem principally from three factors: (1) a small decline resulting from decreased expenditure of human energy associated with labor-saving devices and motorized travel, (2) a fairly widespread and gradually rising standard of living associated with the inclusion of higher proportions of certain more expensive foods largely of animal origin in place of breadstuffs and (3) a higher per capita consumption of sugars and sweets and of fats exclusive of butter. Preservation of health demands that the last-mentioned factor be carefully watched, since this trend may increase incidence of obesity and associated diseases. Proper use of foods such as flour and bread which carry important protective food substances must be preserved.

Current Comment

MORBIDITY AND MORTALITY STATISTICS OF DOMESTIC ANIMALS

Reliable morbidity and mortality statistics of domestic animals are unavailable. The veterinarian is required to report certain communicable diseases, but reporting is uncertain and enforcement difficult. The incidence of numerous other diseases is entirely unknown—diseases of great economic importance as well as diseases which may be transmitted to man. The United States Livestock Sanitary Association, the American Veterinary Medical Association and the Division of Biology and Agriculture of the National Research Council have interested themselves in the problem, with the hope that proper legislation may be enacted to correct the situation. The United States Bureau of Animal Industry is cognizant of the need but has neither the funds nor the personnel to initiate the program. The consensus seems to favor compulsory reporting to the office of the state livestock disease control official and thence to the United States Bureau of Animal Industry, with possibly the establishment of a new division of vital statistics.[1] Numerous problems must be solved before the project can be functionally effective. Manuals on nomenclature and on standard methods of diagnosis are in process of preparation but are not yet available. Experiments in the collection of morbidity and mortality data of farm animals have been made in a small way, and should be continued. The shortage of veterinary pathologists will require some years to remedy. The seriousness of the problem, however, from both the economic and the public health point of view, as well as the possible role that infectious diseases of animals might play in biologic warfare, calls for serious attention.

1. Schroeder, C. R.; Buzzell, F. G.; Foote, R. E.; Good, G. H.; Hurt, L. M.; Newton, R. C., and Schneider, A. P.: Report of the Committee on Morbidity and Mortality Statistics, Proc. U. S. Livestock and Sanitary A., December 1947, pp. 228-238.

INTERNATIONAL TUBERCULOSIS PREVENTION

Under the sponsorship of the United Nations International Children's Emergency Fund and the Danish, Norwegian and Swedish Red Cross, a program for tuberculosis control on an international basis is being established.[1] The program which is to be carried out in war-ravaged countries of Europe envisages examination of 50,000,000 children and adolescents under 18 years of age. An estimated fifteen million of these children, the report states, will be found to need and will be given BCG vaccine. The bulk of the funds needed ($4,000,000) will be contributed by the United Nations International Emergency Children's Fund, and additional sums are expected from other cooperating organizations. The World Health Organization will provide technical advice and assistance. "Joint enterprise" agreements will be signed between the sponsors and the Ministry of Health of each participating country. Medical teams for actual work will be assembled in each country, composed of nationals and medical personnel supplied by the sponsoring agencies. Fresh vaccine and tuberculin will be supplied by the Danish State Serum Institute until each country is able to supply its own. Tuberculin intradermal or patch tests will be performed on all children, and positive reactors will be vaccinated with BCG. Presumably BCG has protective value for several years. Technical direction of the program is being entrusted to Danish, Norwegian and Swedish personnel because these countries have highly developed the technics of mass vaccination with BCG during the past twenty years ("The tuberculosis death rate in Denmark in 1947 was 30 per 100,000 inhabitants."[1]) Death rates in some of the countries to be included in the program are at least ten times the Danish rates. Joint enterprise agreements have already been signed in Finland, Hungary, Czechoslovakia, Poland and Yugoslavia. In Central Europe alone, as of July 1, 1948, more than 2,000,000 persons have been tested and over 600,000 vaccinated. China, Greece and Italy, as well as other countries of Asia and Western Europe, are being considered for extension of the program. The sponsors of this campaign, realizing that vaccination alone is not sufficient, consider other measures necessary for success to be expansion of public health services for detection of new cases of tuberculosis, furnishing of increased numbers of beds for isolation purposes and training of more adequate numbers of personnel. The program is truly international in that neither national borders nor political, racial nor religious discrimination will interfere with the extension of the program to the war-ravaged areas where greatest need exists.

1. The What, How and Why of the International Tuberculosis Campaign, Public Relations Office, International Tuberculosis Campaign, Copenhagen, Denmark, 1948.

ORGANIZATION SECTION

Official Notes

COUNCIL ON MEDICAL SERVICE

Southeastern Regional Conference

The Southeastern Regional Conference on Medical Service for 1948 was held at the Columbia Hotel in Columbia, S. C., on October 12 and 13. The Conference met in 1946 and 1947 in Atlanta.

The meeting was opened with an address of welcome by Dr. R. B. Durham, president of the South Carolina Medical Association.

The Tuesday session was devoted to "Rural Medical Service." Mrs. Wilma B. Sledge, social and educational director for the Mississippi State Farm Bureau Federation, discussed "Rural Health Problems and Methods of Their Solution." She gave an interesting résumé of the problems in health of the rural population of Mississippi and of the steps which have been inaugurated and are now in progress toward meeting them. She emphasized the extent to which the shortages of hospital facilities, nurses' and physicians' services are inseparably related to one another and to the shortage of financial resources, in preventing the rendition of totally adequate service.

Dr. William R. Pretlow of Warrenton, Va., discussed the operation of medical and hospital prepayment plans in rural communities. One of the founders of Virginia Medical Service (the medical prepayment plan in Virginia) and now a member of its board of trustees, Dr. Pretlow, who practices in what he described as one of the most completely rural counties of Virginia, showed how the nonprofit prepayment plans, designed to make medical and hospital service more available to the lower income group, could be made to operate on a sound, satisfactory and practical basis in farming areas as well as in the urban centers of population.

Dr. R. V. Platou, head of the department of pediatrics in the Medical School of Tulane University, described the type of survey now being conducted by him and his associates at Tulane, throughout ten counties in southern Mississippi, to determine the extent of the availability of medical care and hospitalization, the existing need and, particularly, the points at which additional medical service and facilities for treatment are essential. Accompanying his remarks with a number of slides showing graphically the findings thus far, Dr. Platou indicated that in the opinion of those engaged in making the survey the matter of supplying the needs would follow more or less automatically once the survey is complete.

The theme of Wednesday morning's program was "Problems of Health in the Southeastern States," and its treatment approached by five speakers from as many different angles.

Dr. C. L. Guyton, head of the division of hospitals of the South Carolina Department of Health, now engaged in administering the program for hospital and health center construction under the terms of the Hill-Burton Act, described in detail what is being done in South Carolina. He pointed out many of the practical difficulties encountered and the minimum requirements that must be met in supplying treatment facilities, if the plan and purpose for which the federal and state funds were appropriated are to be accomplished.

Miss Katherine Edwards, now principal of the elementary schools of Greenville, S. C., spoke of the practical side of health problems among school children. From her own experience, Miss Edwards made it clear that a teacher alert to the reaction of her pupils can generally tell when all is not right with their health, and that the teacher should be encouraged to concentrate on detecting illness and lending her aid in the improvement of the child in this respect as well as in mental training. The chief emphasis of her discussion was on the fact that problems of this sort will have to be solved primarily by two groups, the teachers and the physicians. Both of these professional groups with background, point of view and occupation so directly related to the physical and social well-being of the people must recognize, she pointed out, and concentrate on discharging the responsibilities for which their training and professional status have fitted them.

Mr. W. Cicero Kendrick of Atlanta, a prominent leader in organized labor and an official of the Georgia State Federation of Labor, pointed out that labor as a group is just as vitally interested as any other in preserving the freedom and independence of the American way of life, and that employees recognize that their welfare depends on the welfare of the employer. This mental attitude, however, and that of other groups, do not alter the fact that many persons, he said, are without adequate medical care and hospital service, through circumstances beyond their immediate control. While he did not favor a system of state medicine such as has often been discussed, he expressed the belief that this might be the ultimate result unless some other solution is found. He called on the medical profession to furnish the leadership in finding such a solution and pledged the cooperation of labor and other lay groups in any movement reasonably calculated to relieve the situation.

Dr. John T. T. Hundley of Lynchburg, Va., presented the results of a survey conducted by him a few months ago, in determining what the lay public generally thinks of the adequacy of available medical care and the things which need most to be changed to improve it. Dr. Hundley, who is a practicing physician specializing in internal medicine, sent requests to a large number of people in various occupations and strata of society, requesting their estimate of doctors and the service rendered by them. Some of the replies he received were enlightening and highly interesting, if not always entirely complimentary. The attitude consistently expressed by the majority of those who replied was favorably inclined toward the medical profession.

Comments on the subject from the standpoint of a Washington observer were given by Dr. Joseph S. Lawrence, of the Washington office of the American Medical Association Council on Medical Service. Dr. Lawrence brought valuable observations regarding the probable future trends. He called attention to the numerous bills introduced in the last Congress, some of which were passed, affecting one phase or another of the subject of medical care for all people.

Dr. Walter B. Martin of Norfolk, Va., a member of the Board of Trustees of the American Medical Association, outlined the steps taken by the national organization within the past few years in its active program to preserve the free system of the practice of medicine. He stressed the Ten Point Program of the American Medical Association, adopted and now in process of execution. This, he believed, if properly activated and extended, should go far toward answering criticism leveled at the profession in the past, and remedy most of whatever defects exist in the system of medical service which has always been a part of democratic free American institutions.

After luncheon at 1 p. m., with members of the Conference guests of the South Carolina Medical Association, the discussion was resumed, the afternoon being devoted to general discussion, led by Mr. Thomas A. Hendricks of Chicago, Executive Secretary of the American Medical Association Council on Medical Service, and Dr. Fred C. Hubbard of North Carolina.

The two day meeting was attended by representatives of the medical associations of North Carolina, Virginia, Georgia, Florida, Tennessee, Louisiana and South Carolina. The total number registered was 53, and the general consensus seemed to be that the program arranged was successful in focusing the thought and presenting prepared discussions on those subjects of most vital interest to the profession, in its quest for an answer to the questions which have been so prominent in the minds of the public for one reason or another during the past few years. No formal action was determined upon and none was proposed by the Conference. The ideas expressed were

for the further consideration of the delegates in their respective state groups and for approval wherever possible, according to the means most adaptable in each area.

The arrangements for the Conference were in charge of a committee composed of Dr. Julian P. Price, chairman; Dr. Walter B. Martin and Dr. H. B. Mulholland, dean of the University of Virginia Medical School, Charlottesville, and a member of the American Medical Association Council on Medical Service. Dr. Mulholland presided at the first day's session and Dr. Price presided on Wednesday. Mr. M. L. Meadors, director of public relations and counsel of the South Carolina Medical Association, and Henry S. Johnson, director of public relations and medical service of the Medical Society of Virginia, took part in the meeting.

Washington Letter

(From a Special Correspondent)

Nov. 22, 1948.

Report of Office of Civil Defense Planning

Medical and public health responsibilities of a home defense program for the United States are sharply defined in the blueprint for organization which has been submitted to Secretary of Defense James Forrestal by the Office of Civil Defense Planning. Its report recommends establishment by Congress of a permanent Office of Civil Defense and subsequent enactment by states and municipalities of supporting laws which would be required to integrate the system.

The director of the proposed Office of Civil Defense would report to the Secretary of Defense or directly to the President. In his 300 page printed report to Secretary Forrestal, Chairman Russell J. Hopley of the Office of Civil Defense Planning said the former is preferable. Four deputy directors are provided for: Plans and Operations, Medical and Health Services and Special Weapons Defense, Technical Services, Training. The medical deputy "should be an outstanding member of the medical profession, licensed to practice medicine and surgery, and have had broad medical and administrative experience."

Under his general supervision wuold be four broad divisions: medical and health services, radiologic defense, chemical defense and "other special weapons defense," the last-named division concerning itself with a subject which is still alluded to only inferentially in government documents — biologic warfare. Bureaus organized similarly would be set up by the several states, cities and metropolitan areas.

"In modern total warfare," says the Hopley report, "the civilian frequently is subjected to enemy attack to an extent comparable to that experienced by the soldier. An attacked civilian population demands the same treatment of casualties and the sick, and protection against communicable diseases that is required by the military forces. In crowded urban areas, deaths, disability and suffering resulting from enemy action can easily exceed any which has ever been experienced by armies. In such instances, unless there is adequate provision for the preservation of the health and lives of the civilian population, the consequent reduction in civilian manpower, working effectiveness and morale will so cripple our industries as to make defeat more than a possibility. There can be no satisfactory civil defense without adequate provision for medical and health defense."

Headed by a physician, the medical and health services division would have three branches: medical care, public health and administration. In peacetime, the branch chiefs might serve on a part time basis, except that administration would be a full time activity, staffed by the Army, during peace as well as war. The public health and medical care services branches are subdivided into specialty sections, the heads of which would serve as consultants in peacetime.

The chief of the radiologic defense division would hold a doctorate degree, preferably in medicine, and should be a career man in government service, says the report. This division would have a five member advisory committee. A medical and health advisory committee also is recommended, its members representing the following organizations: Red Cross, National Research Council, American Medical Association, American Dental Association, American Association of Industrial Physicians and Surgeons, American Public Health Association, Association of State and Territorial Health Officers, American Veterinary Medical Association, American Nurses Association, American Hospital Association, Catholic Hospital Association, American Protestant Hospital Association and the American Pharmaceutical Association.

In making the Hopley report public, Secretary Forrestal explained that he wished to stimulate general discussion of the issue even before details of the plan are approved by his and other government agencies. Mr. Hopley, in a letter accompanying transmittal of the report to state governors, said in part:

"While my own planning group is naturally convinced of the soundness of its recommendations, it is obvious that a report which concerns the entire civilian population and is of interest to so many governmental agencies must be subjected to the most careful scrutiny and review before it can finally be approved. . . . When all these comments have been received and considered, the report in its present form, or as modified as a result of such consideration, will be referred to the President for approval and subsequent submission to the Congress."

Dr. Perrin H. Long, professor of preventive medicine at Johns Hopkins University School of Medicine, served as medical advisor to the Office of Civil Defense Planning. Its consultant in radiologic defense was Dr. George M. Lyon, of Veterans Administration. Each was assisted by an advisory committee.

The report, whose 300 pages of text are supplemented by 17 organizational charts and proposed model legislation on federal, state and local levels, is purchasable ($1) from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

"Keto-Bemidone" Held Too Dangerous for Clinical Use

After investigation of the drug at the U. S. Public Health Service special hospital at Lexington, Ky., the Committee on Drug Addiction and Narcotics, National Research Council, has advised the Bureau of Narcotics and Food and Drug Administration that K-4710, "keto-bemidone" (4-[metahydroxypheny]-1-methyl-4-propionyl piperdine hydrochloride) has addictive properties too great to justify its distribution as an analgesic. The drug was submitted for assay last January by Winthrop-Stearns, Inc.

Coming Medical Meetings

American Medical Association Interim Session, St. Louis, Municipal Auditorium, Nov. 30-Dec. 3. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Annual Conference of State Secretaries and Editors, St. Louis, Hotel Statler, Nov. 28-29. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

National Medical Public Relations Conference, St. Louis, Hotel Statler, Nov. 27. Mr. Lawrence W. Rember, 535 N. Dearborn St., Chicago 10, Director.

American Academy of Allergy, Atlantic City, Chalfonte-Haddon Hall, Dec. 6-8. Dr. Theodore L. Squier, 425 E. Wisconsin Ave., Milwaukee 2, Secretary.

American Academy of Dermatology and Syphilology, Chicago, Palmer House, Dec. 5-9. Dr. Earl D. Osborne, 471 Delaware Ave., Buffalo, Secretary.

American Society of Tropical Medicine, New Orleans, Roosevelt Hotel, Dec. 5-9. Dr. Frederick J. Brady, National Institute of Health, Bethesda 14, Maryland, Secretary.

Association for Research in Nervous and Mental Diseases, New York, Waldorf-Astoria Hotel, Dec. 10-11. Dr. Clarence C. Hare, 700 W. 168th St., New York 32, Secretary.

Eastern Section, American Federation for Clinical Research, Philadelphia, Temple University School of Medicine, Dec. 4 Dr. J. Edward Berk, Temple University School of Medicine, Philadelphia, Chairman.

Puerto Rico, Medical Association of, Santurce, Dec. 10-12. Dr. J. Basora Defillo, Box 3866, Santurce, Secretary.

Radiological Society of North America, San Francisco, Dec. 5-10. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse 2, N. Y., Secretary.

Southern Psychiatric Association, Dallas, Texas, Hotel Adolphus, Dec. 6-7. Dr. Newdigate M. Owensby, 384 Peachtree St. N.E., Atlanta, Ga., Secretary.

Southern Surgical Association, White Sulphur Springs, W. Va., Dec. 7-9. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Western Surgical Association, St. Louis, Dec. 2-4. Dr. Warren H. Cole, 1853 W. Polk St., Chicago 12, Secretary.

GOVERNMENT SERVICES

SELECTIVE SERVICE SYSTEM

EDUCATIONAL ADVISORY COMMITTEE

The Director of Selective Service, Washington, D. C., issued on November 2 a memorandum to all local boards outlining the recommendations of the National Headquarters with respect to the deferment of preprofessional and professional students. This memorandum announced that the Director had established a Healing Arts Educational Advisory Committee, the purpose of which is to recommend means by which sufficient personnel may be trained in the healing arts, through the maintenance of an adequate flow of students through professional and preprofessional schools; to recommend procedures by which an adequate flow of students through the professional schools might be maintained to meet the nation's needs in trained medical, dental, veterinary and osteopathic personnel, and to advise the educators on problems arising through the operation of the Selective Service Act of 1948.

The Committee consists of Donald G. Anderson, M.D., representing the Council on Medical Education and Hospitals of the American Medical Association, Stockton Kimball, M.D., representing the Association of American Medical Colleges, G. D. Timmons, D.D.S., representing the Association of American Dental Schools, Dr. B. T. Simms, D.V.S., representing the American Veterinary Medical Association, and Otterbein Dressler, D.O., representing the American Osteopathic Association.

Students in Professional Schools: The Committee has advised the Director of Selective Service that the national interest will require graduates of medicine, dentistry, veterinary medicine and osteopathy annually in numbers equal at least to the present level. It recommends that students properly enrolled in the professional schools of these four professions and satisfactorily pursuing full time courses leading to graduation should be permitted to continue their studies until graduation.

Students in Preprofessional Schools: The Committee also recommends that sufficient numbers of preprofessional students be made available to maintain the freshman classes of these professional schools at present levels. To accomplish this the Committee recommends that these professional schools select provisionally for admission, on completion of the preprofessional course to the satisfaction of the professional school, certain students who have satisfactorily completed at least one year of the preprofessional course. These provisional admissions will continue valid until the following July 15 unless cancelled by the professional school.

The number of preprofessional students who are not otherwise deferable and who have completed at least one year of preprofessional work and who may be selected, is, for the freshman class of 1949, 55 per cent of the 1948 freshman professional class; for the freshman class of 1950, 62½ per cent of the 1948 freshman professional class, and for the freshman class of 1951, 100 per cent of the 1948 freshman professional class.

These percentages of provisional admissions are to be reviewed by the Committee once each year, and recommendations as to the numbers will be adjusted for the ensuing classes in accordance with the demonstrated needs at that time.

Identification of Professional Students and Preprofessional Students Provisionally Accepted: To identify to local Selective Service Boards the professional students of medicine, dentistry, veterinary medicine and osteopathy, and the preprofessional students who have been provisionally admitted to the professional schools, the Committee has recommended that an authorized representative of the professional schools should submit, on a form designed for that purpose, (1) the names of professional students who are not otherwise deferrable under the Selective Service Act of 1948 and who have duly matriculated in their professional schools and are actually pursuing a course leading to graduation in one of the specified professions and (2) the names of preprofessional students who have completed at least one year of preprofessional study and have been provisionally accepted for entrance into the professional school on completion of a preprofessional course to the satisfaction of the professional school.

Certification of Preprofessional and Professional Students: The form to be used by the professional schools will be Certification of Preprofessional and Professional Students of Medicine, Dentistry, Veterinary Medicine and Osteopathy (SSS form no. 103). Such certificates will be issued to local boards through national headquarters and state headquarters for Selective Service, and will constitute evidence in support of the student's claim for occupational classification. Before issuing a certificate for a preprofessional student, the professional school should secure assurance from the student that he will not obtain a similar certificate from another professional school.

Failure to Pursue Course of Study Satisfactorily: When a student fails to pursue his course satisfactorily to the professional school, an authorized representative of the school will cancel the Certification of Preprofessional and Professional Students of Medicine, Dentistry, Veterinary Medicine and Osteopathy (SSS form no. 103) and will notify the local board of such cancellation, through national headquarters and state headquarters of Selective Service.

NAVY

COUNCIL ON RADIO-BIOLOGICAL RESEARCH

The Council on Radio-Biological Research of the Bureau of Medicine and Surgery recently held its first meeting at the Naval Medical Research Institute, Bethesda, Md. Captain R. H. Draeger, M.C., U.S.N., head of the Research Branch, Atomic Defense Division, Bureau of Medicine and Surgery, acted as chairman. Representatives from the Office of the Surgeon General of the Army, the Armed Forces Special Weapons Project, U. S. Atomic Energy Commission, Naval Radiologic Defense Laboratory, Office of Naval Research and Naval Medical Research Institute were present. The function of this council is to review all proposed research projects in the fields of radiation biology, diagnosis and therapy of radiation illness, internal radiation hazards and methods of photographic dosimetry and personnel decontamination; to assign equitable priority to such projects, and to recommend such projects to the proper laboratory for investigation.

TRAINING IN CIVILIAN INSTITUTIONS

The following lieutenants (jg) of the Medical Corps Reserve have been ordered to active duty at civilian medical institutions as interns under the Medical Training Program: William C. Adams Jr., of Boise, Idaho, to St. Johns Hospital, Santa Monica, Calif.; Frederick Brockmeier of Glendale, Ohio, to Christ Hospital, Cincinnati; William B. Buckingham of Oak Park, Ill., to Cook County Hospital, Chicago; John L. Falls of River Forest, Ill., to Cook County Hospital, Chicago; Richard R. Grayson of Maywood, Ill., to Cook County Hospital, Chicago; Rice T. King of Jacksonville, Fla., to Baltimore City Hospitals, Baltimore; William H. Kittrell of Mt. Pleasant, Tenn., to Philadelphia General Hospital, Philadelphia; Martin H. Klein of Fountain City, Wis., to City Hospital of Akron, Akron, Ohio; Robert S. Meador of Leonard, Texas, to Scott and White Hospital, Temple, Texas; Hale B. Soyster Jr., of Los Angeles, to Los Angeles County General Hospital; Harold E. K. Sweeny of Elizabeth, N. J., to Wesley Memorial Hospital, Chicago;

Edward E. Tennant of Cleveland to Christ Hospital, Cincinnati; John F. Westfall of Glendale, Ariz., to Gallinger Municipal Hospital, Washington, D. C.; Jack S. Woodruff of Columbus, Ohio, to Indianapolis City Hospital, Indianapolis, and Belton J. Workman Jr., of Woodruff, S. C., to Roper Hospital, Charleston, S. C.

NAVAL OFFICERS AWARDED MEDAL AND PRIZE

The Association of Military Surgeons of the United States recently announced that two officers of the Naval Medical Research Institute, Bethesda, Md., had been awarded the Sir Henry Wellcome Medal and Prize. The recipients are Lieut. Comdr. Eugene P. Cronkite, M.C., U.S.N., and Lieut. (jg) William H. Chapman, M.S.C., U.S.N. Their paper, "A Critical Analysis of the Syndrome of Acute Total Body Radiation Illness," was selected by the association as the best submitted in the annual competition. The honorarium and scroll accompanying the award were presented by Brig. Gen. Edgar Erskine Hume, U.S.A., president of the association, November 12 at the annual convention in San Antonio, Texas. Dr. Cronkite is head of the Hematology Facility, Naval Medical Research Institute, and Lieutenant Chapman is a member of the staff.

CLINICAL PSYCHOLOGISTS WANTED FOR REGULAR CORPS

Applications are desired from Naval Reserve officers who hold the Ph.D. in psychology, or have completed all course work for this degree, for transfer to the regular navy, medical service corps (clinical psychology). Officers who are accepted for appointment will be assigned to clinical psychology billets, neuropsychiatry service in continental Naval hospitals, Naval and Marine training centers, retraining commands, and disciplinary barracks. Previous military experience in psychology is not a requisite; however, preference will be given to reserve officers who filled psychologic billets during World War II. Applications should be initiated through the Naval districts in which the applicant resides; however, more detailed information can be secured from the Navy Department, Bureau of Medicine and Surgery, Attention: Professional Division, Washington, D. C.

RETIRED OFFICERS REQUEST ACTIVE DUTY

The following retired medical officers have requested recall to active duty: Capt. Harold A. Noreen, Minneapolis, to 9th Naval District as assistant to the district medical officer in connection with the Medical Reserve Program; Comdr. Norman J. Haverly, Long Beach, Calif., to the Office of Naval Office Procurement, Los Angeles, and Comdr. Esdras J. Lanois, Cleveland, to the Administrative Command, Naval Training Center, San Diego, Calif., for duty in the Medical Department.

NEW NAVY INTERNS

The Bureau of Medicine and Surgery announced October 27 that thirty-two additional lieutenants (jg) in the Medical Corps Reserve have reported for their first active duty in internships at various civilian medical institutions under the Navy Medical Training Program. These officers will serve on active duty in the Navy after completion of their internships.

AWARDS AND COMMENDATIONS

Lieutenant Arlington Bensel Jr.

Lieutenant Arlington Bensel Jr., U.S.N.R., of East Orange, N. J., has been authorized by the Navy Department to wear the Presidential Unit Citation ribbon with star by virtue of his service with the First Marine Division, which was cited by the President of the United States "for extraordinary heroism in action against enemy Japanese forces at Peleliu and Ngesebus from Sept. 15 to 29, 1944."

PERSONALS

Lieutenant (jg) Frank R. Johnson of LaGrange, Ill., has accepted appointment in the Regular Navy Medical Corps and has been nominated for duty under instruction in a residency in surgery at the Presbyterian Hospital, Chicago.

Lieut. (jg) Harry C. Alfred of St. Joseph, Mo., will report for his first active duty in the Medical Corps Reserve at the Naval Hospital, Memphis, Tenn.

Lieutenant (jg) Nathaniel M. Cohen Jr., Brookline, Mass., has transferred from the active reserve to the regular navy.

VETERANS ADMINISTRATION

DOCTORS NEEDED IN TUBERCULOSIS HOSPITALS

One hundred full time doctors are needed by Veterans Administration for duty in its tuberculosis hospitals. Applicants should address their inquiries to the Chief Medical Director, Veterans Administration, Washington 25, D. C. The openings are scattered throughout the nation among Veterans Administration hospitals specializing in the treatment of tuberculous veterans and in Veterans Administration general hospitals operating tuberculosis departments.

The salary scale for full time doctors in the Veterans Administration's Department of Medicine and Surgery ranges between $4,479 and $10,305 annually for jobs now open. During the past year, 18,222 tuberculous veterans were admitted to Veterans Administration hospitals for treatment. Discharges during the same period totaled 18,071.

SITE FOR NEW HOSPITAL AT CLEVELAND

The Administrator of Veterans Affairs, Carl R. Gray Jr., has authorized the acquisition of twenty acres of land at Cleveland for a 1,000 bed veterans general hospital. The tract, which is less than a mile from the Western Reserve University Medical School, now has on it fifteen mansion type dwellings, some of which will be used as auxiliary hospital buildings. The City Council, it is said, will vacate the portion of Magnolia Drive lying within the perimeter of this tract and relocate all utilities lying in the bed of the street.

PERSONALS

Dr. Edward S. Post has become manager of the Veterans Hospital at Battle Creek, Mich., succeeding Dr. Roger P. Hentz.

Dr. William S. Schwartz of Portsmouth, Ohio, has become chief of professional services at the Veterans Administration hospital units at Oteen and Swannanoa, N. C. Dr. Schwartz formerly was chief of tuberculosis services at the veterans hospital at Brecksville, Ohio.

Dr. Arthur J. Klippen, chief medical officer at the Saginaw, Mich., subregional district office of the Veterans Administration, has been appointed chief of professional service with offices in Detroit. Dr. Klippen resigned as secretary of the Saginaw County Medical Society on acceptance of his new post and will move to Detroit. He was a lieutenant colonel in the Army Medical Corps during the recent war.

E. Burns Geiger, formerly of Hagerstown, Md., has been appointed chief of the Pharmacy Division of the Veterans Administration Department of Medicine and Surgery. Mr. Geiger served in the Navy during the war and later became assistant to the chief of the Division of Pharmacy.

HOSPITAL NEWS

The Veterans Administrations announces that the contract for the construction of a 131 bed addition to the Veterans Administration hospital at Brecksville, Ohio, has been awarded for $937,000.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARKANSAS

Dr. Roberts Resigns as Dean.—Dr. Joseph T. Roberts, University of Arkansas School of Medicine, Little Rock, has resigned as dean and head of the department of medicine. Dr. William C. Langston, assistant dean and professor of anatomy, has been named acting dean. Dr. Langston, a graduate of the State University of Iowa College of Medicine, Iowa City, 1929, has been on the faculty of the school since 1930.

Narcotic Violation.—According to the Bureau of Narcotics, Dr. James H. Cole, Morrilton, pleaded guilty in the U. S. District Court at Little Rock August 30 to a charge of violating the federal narcotic code, and on that date was sentenced to serve a term of five years and thereafter will be placed on probation for a like period, with the provision that he should not practice medicine in any form.

CALIFORNIA

Society News.—Dr. Paul H. Pernworth, Compton, addressed the Southeastern Branch of the Los Angeles County Medical Association, November 3, on "Therapeutic Applications of Regional Anesthesia." The Los Angeles Obstetrical and Gynecological Society elected Drs. L. Grant Baldwin, president, and Gordon Rosenblum, secretary-treasurer, for the coming year.

Dr. Starr Appointed Acting Chairman of Department.—Dr. M. Paul Starr, clinical professor of medicine of the graduate division of the University of Southern California School of Medicine, Los Angeles, has been appointed professor and acting chairman of the department of medicine. Dr. Starr came to the university in 1945 after serving in the Army Medical Corps. He is a graduate of Rush Medical College, 1922, and beginning in 1924 he served on the staff of Northwestern University School of Medicine.

COLORADO

Courses for General Practitioners.—A course for general practitioners in Colorado and neighboring states will be conducted at the University of Colorado Medical Center, Denver, between December 13 and 17, through the joint sponsorship of the Colorado State Medical Society and the University of Colorado School of Medicine. This course is planned to give general practitioners instruction in recent developments in the diagnosis and treatment of diseases involving the cardiovascular and gastrointestinal systems, as well as disorders connected with endocrines, metabolism, the hemopoietic system and the chest. Fifty per cent of the time will be given to free discussion and presentation of questions by the participants. The course is open to licensed physicians in the Rocky Mountain region in general who are members of their respective state medical societies. A registration fee is required of all applicants. The tuition is $20. Interns and residents are invited to register and take part in the course without charge. Director of the course is Dr. Robert S. Liggett, professor of medicine.

A course in anesthesiology for general practitioners will be given at the Medical Center, January 12-15, 1949, sponsored by the Colorado State Medical Society, the Colorado State Society of Anesthesiologists, the University of Colorado School of Medicine and the Denver Society of Anesthesiologists. Except for interns, eligibility and fees are the same as for the course in general medicine. The director of the course is Dr. Philip A. Lief, associate professor of anesthesiology. For information, write the Director of Graduate and Postgraduate Medical Education, University of Colorado Medical Center, Denver.

CONNECTICUT

Professor Watkins Dies.—Professor John H. Watkins, Ph.D., associate professor of public health at Yale University and associated with the university since 1928, died in New Haven September 25, aged 47.

Personals.—Dr. Adrian C. Moulyn of the Yale Plan Clinic at New Haven has been appointed staff psychiatrist of the new clinic for the care and treatment of alcoholic addicts at Stamford, Conn. Dr. Moulyn is a graduate of the medical school of the University of Utrecht, Holland, in 1930. He has been an instructor in psychiatry and mental hygiene at Yale University School of Medicine.——Dr. Francis L. Lundborg, West Hartford, was appointed medical director at Trinity College succeeding Dr. Horace C. Swan, Hartford, who retired in June. Dr. Lundborg, a graduate of Yale Medical School, New Haven, 1930, formerly assisted Dr. Swan in the health program for Trinity students.

Yale Library Opens to State Physicians.—Medical reference material formerly limited to Yale medical students and faculty has been made available to Connecticut physicians through the recent creation of the Associates of the Yale Medical Library. More than one hundred and sixty physicians have become associates since the group's inception two months ago. Invitations to membership are being sent to Connecticut doctors and Yale medical alumni throughout the nation. The associates are granted borrowing privileges of the library and will receive its bulletins including accession lists and notices of important meetings. To expand further the facilities and services of the library the associates will pay a small annual subscription fee and are urged to contribute books and other material that will enhance the library. Officers of the associates are Dr. Herbert Thoms, chairman, Dr. Levin L. Waters, secretary, Laurence G. Tighe, treasurer, all of New Haven, and Dr. George Blumer, San Marino, Calif., former dean of the school of medicine, honorary chairman.

Silver Hill Foundation Medical Council Meeting.—At the annual meeting of the Silver Hill Foundation Medical Council in New Canaan in October, the subject for discussion was "What is the Ideal Method of Treating the Psychoneuroses, Psychosomatic Illnesses and Psychosocial Disorders?" Speakers were Drs. Harold L. Amoss, Greenwich; Arlie V. Bock, Boston; Walter O. Klingman, Charlottesville, N. C.; Fredrick C. Redlich, New Haven, and Edwin G. Zabriskie, New York. The Silver Hill Foundation is a psychotherapeutic unit devoted to the study, care and treatment of the psychoneuroses where patients are given brief, intensive psychotherapeutic and physiologic aid. The medical staff is composed of internists who, although they are specialists certified by the American Board of Psychiatry and Neurology, are interested in the eclectic approach to the treatment of the psychoneuroses rather than adhering to any one formal school of psychiatry. The medical director of the foundation is Dr. William B. Terhune of New Canaan and New York. Members of the council are outstanding physicians from various sections of the country.

DISTRICT OF COLUMBIA

Borden Lectures Revived.—Dr. John McMichael, professor of medicine at the University of London, delivered the William C. Borden Lecture November 15 at George Washington University School of Medicine. Dr. McMichael's address, "Some Peripheral Vascular Reactions of Surgical Interest," revived the Borden lectures, which were discontinued during the war. The lectures are made possible by a fund established by the Borden family in memory of the late Dr. William C. Borden, formerly dean of the medical school. Dr. McMichael has recently returned from a lecture tour of the United States and Canada. In addition to being professor of medicine at the University of London, Dr. McMichael is professor of medicine at the British Post-Graduate Medical School and chief of medicine at the Hammersmith Hospital in London.

ILLINOIS

Lecture on Atomic Injuries.—The Peoria County Medical Society in conjunction with the 203d Medical Battalion, Illinois National Guard, will have a dinner and lecture December 7 in the Pere Marquette Hotel, Peoria, at 8 p. m. Lieut. Col. John R. Hall Jr., U. S. Army Medical Corps, and former X Corps Surgeon in Japan, will speak on "Treatment of Atomic Bomb Injuries." All physicians and medical officers of the guard are invited.

Tuberculosis Mortality at Record Low.—The Illinois State Department of Public Health reports that mortality from tuberculosis in the state in 1947 was lower than in any previous year of record. The death rate of 33.6 per 100,000 population was about 9 per cent below that for 1946. During the past two decades mortality reports show that tuberculosis has declined by more than 50 per cent. In 1927 the rate was 74.9, and in 1937 it had dropped to 44.2 per 100,000 population. The State Department of Public Health has placed in operation seven mobile x-ray units, through which service more than 250,000 persons received roentgen examinations of their chests in 1947. Many additional units are also being operated in the state by local official and voluntary health agencies. To provide additional facilities for the care of tuberculosis patients, the state

has developed plans and appropriated funds for the construction of two new sanatoriums: one of 100 bed capacity to be located at Mt. Vernon and another of 500 bed capacity to be located in Chicago.

Chicago

Dr. Cannon Receives Awards.—Dr. Paul R. Cannon, professor and head of the department of pathology at the University of Chicago, recently received two awards, the William Wood Gerhard Gold Medal of the Pathological Society of Philadelphia for outstanding work in medical research and the Ward Burdick Award-Medal of the American Society of Clinical Pathologists for outstanding contributions to pathology. Dr. Cannon received his medical degree in 1925 from the Rush Medical College.

Society News.—At the meeting of the North Side Branch of the Chicago Medical Society at the Drake Hotel December 2, Dr. Mayo H. Soley, dean and research professor in clinical medicine, State University of Iowa College of Medicine, Iowa City, will speak on "Present Status of Radioactive Iodine in Treatment of Toxic Goiter." The second address will be given by Dr. Paul S. Rhoads of Northwestern University Medical School, on "Inhalation of Penicillin Dust: Its Role in Respiratory Diseases."

Tons of Dust Per Square Mile.—During September Chicago air contained less dust than during any other month since the city began recording dust fall in 1926, according to the city's smoke inspector. The average dust fall was 34.65 tons per square mile, compared with the previous low of 36.5 tons in December 1940. The average was 51.53 tons in September 1947 and 41.1 tons in August 1948. The average soot fall in September was 9.26 tons, compared with 7.56 in August. The decline in dust fall is attributed in part to the campaign to curtail railroad and factory smoke.

Drs. Ivy and Youmans Cited for Wartime Service.—Dr. Andrew C. Ivy, vice president of the University of Illinois, received the president's certificate of merit, and Dr. John B. Youmans, dean of the college of medicine, the Army and Navy certificate of merit, November 6. The certificates are given in recognition for the wartime services of distinguished scientists and engineers of the Office of Scientific Research and Development. Major General John F. Lucas, deputy commander of the Fifth Army, and Captain Phillip G. Stokes, commandant of the Naval R.O.T.C. at the University of Illinois, presented the certificates.

Research Grants to Illinois.—The University of Illinois College of Medicine has been awarded the following grants for research: Office of the Surgeon General, Department of the Army, has awarded a $10,000 grant for the "Pharmacodynamic Study of Renal Blood Flow," to be conducted by the department of pharmacology, under the supervision of Dr. Jules H. Last. The U. S. Public Health Service has awarded the college of medicine separate grants of $6,000 and $5,500 for visual education depicting clinical manifestations of uterine carcinoma to be undertaken under the supervision of Dr. Frederick H. Falls in the department of obstetrics and gynecology, and for a study of the physiologic effects of the influenza virus on the mammalian host to be conducted under the supervision of Dr. John E. Kempf in the department of bacteriology. A $5,000 grant has been received from Parke, Davis and Company for the development and evaluation of antihistamine and adrenergic blocking agents under the supervision of Earl R. Loew, Ph.D., in the department of pharmacology. A research project on "urogastrone" will be conducted by the department of clinical science through a grant of $3,960 from Ayerst, McKinnon and Harrison, Ltd., under the supervision of Dr. Morton I. Grossman.

KENTUCKY

Hospital News.—Work on the Our Lady of Peace Hospital in Louisville, which is expected to cost more than $2,000,000, was begun in September. It is the first of fifteen projects approved for Kentucky under the federal hospital survey and construction program. The hospital will be operated by the Sisters of Charity of Nazareth.

LOUISIANA

Establish Musser Lectureship.—The Tulane University of Louisiana School of Medicine, New Orleans, will annually sponsor a series of lectures at the university in honor of the late Dr. John H. Musser, who served for more than twenty years as professor of medicine. The first lecture was held November 12, when Dr. John McMichael of the Postgraduate Medical School of London, England, spoke on "The Principle of Venous Pressure Reduction in the Treatment of Congestive Heart Failure." The university plans to hold lectures twice a year, bringing to New Orleans international figures in medical science.

MICHIGAN

Study of Venereal Disease Control.—A new research study in case finding in venereal disease control is being conducted under the joint sponsorship of the Michigan Department of Health and the U. S. Public Health Service, with the cooperation of the local health departments of the state. The object is to find out what is wrong with the current methods of case finding. The study is set up so that within twenty-four hours after a patient with venereal disease has been interviewed at the Michigan Rapid Treatment Center at Ann Arbor or the Social Hygiene Clinic, Detroit, investigations of the contacts can begin. Research began November 1 and will continue until June 30, 1949.

MISSOURI

Personal.—Dr. Edward H. Dunn, St. Louis, now a resident physician at the Veterans Administration Hospital, Jefferson Barracks, has been appointed for missionary service in Fort Yukon, Alaska, where he will be in charge of the Hudson Stuck Memorial Hospital. Dr. Dunn is a graduate of the Washington University School of Medicine, St. Louis, 1943, and served in the Medical Corps from 1944 to 1946.

Public Health Scholarship Fund.—A drive for funds to establish a public health scholarship in honor of Dr. Joseph F. Bredeck is being organized by friends and associates of the late St. Louis health commissioner. Dr. Joseph C. Peden, Missouri Theater Building, St. Louis, who has agreed to head the committee to direct the fund raising, said that the proposed scholarship would be used to train qualified youths in public health administration. Dr. Bredeck died October 4.

NEW YORK

Seminar in Urology.—The American Urological Association through the northeastern section of the country will conduct an intensive postgraduate course in urology Jan. 3-8, 1949 under the auspices of the University of Buffalo School of Medicine. The anatomy, physiology, bacteriology, biochemistry and pathology of the urinary tract will be covered by teachers and clinicians from various clinics throughout the country. For information, write Dr. George E. Slotkin, Chairman, Medical Center Building, 333 Linwood Avenue, Buffalo 9, N. Y.

Roentgen Program in Hospitals.—In upstate New York there are one hundred and sixty-five general, nonprofit hospitals eligible to participate in the State Department of Health program of routine chest roentgen examination of persons admitted. Hospitals with 4,000 admissions or over are eligible to receive the loan of photoroentgen equipment and are paid 50 cents for the report of each admission roentgen examination. Hospitals of less than 4,000 admissions annually use their own equipment and receive $1 for each report. There were twenty-three hospitals participating in the program October 1; fifteen have annual admissions of 4,000 or more each, totaling 128,946 admissions, and eight have less than 4,000 annual admissions, each totaling 17,310 admissions. Applications have been approved and equipment purchased for loan to another sixteen eligible hospitals, and eight others are in the process of being approved. Of one hundred and sixty-five eligible general hospitals in upstate New York forty-seven are participating, are awaiting equipment or have made application.

New York City

Brickner Lecture on Cancer.—The fifteenth Walter M. Brickner Lecture will be given at the Hospital for Joint Diseases by Dr. Peyton Rous of the Rockefeller Institute for Medical Research December 9 at 8:30 p. m., on "Cancer as Accident."

Dr. Gerard to Give Gregory Lecture.—Dr. Ralph W. Gerard, professor of physiology, University of Chicago Medical School, will speak on "Physiology and Psychiatry" in the annual Monas S. Gregory lecture to be sponsored by New York University College of Medicine November 8 at 4 p. m. in the amphitheater of the Psychiatric Division of Bellevue Hospital.

Dr. Sheehan Appointed Scientific Director.—Dr. Donal Sheehan, formerly director of the Commonwealth Fund, has been appointed chairman of the Scientific Committee, New York University–Bellevue Medical Center, and professor and chairman of the department of anatomy at the New York University College of Medicine. He will direct the over-all program of teaching and research to be carried out at the center. Dr. Sheehan was a member of the faculty for ten years before assuming the directorship of the Commonwealth Fund a year ago. From September 1937 to October 1947 he was professor and chairman of the department of anatomy. He was one of the principal authors of the survey report in which was first outlined the plans for the medical center.

Laboratory of Nuclear Studies.—A $2,000,000 laboratory of nuclear studies was dedicated October 7 at Cornell University. It consists of the main building and a structure housing a 300-Mev synchrotron. There will be a staff of 18 faculty members, 24 other full time staff members, 11 graduate research assistants, and 6 part time or temporary technicians under the direction of Robert R. Wilson, Ph.D. The laboratory of nuclear studies was established in 1946 with Robert F. Bacher, Ph.D., as director. Dr. Wilson succeeded Dr. Bacher when the latter was appointed a member of the Atomic Energy Commission.

Schoenberg Lecture on Glaucoma.—Dr. John N. Evans of Brooklyn will deliver the Mark J. Schoenberg Memorial Lecture on "Circulatory Aspects of the Glaucoma Problem" at the New York Academy of Medicine, December 6 at 8 p. m., under the joint sponsorship of the New York Society for Clinical Ophthalmology and the National Society for the Prevention of Blindness. The lectureship was established as a memorial to Dr. Schoenberg's interest and original work in the control of glaucoma. The lecture will be preceded by an illustrated talk on "Observations on the Anterior Chamber Angle with the Gonioprism" by Dr. Harvey E. Thorpe of Pittsburgh.

Personals.—Dr. Robert Gutierrez recently returned from a lecture trip to South America, where he conducted operative clinics in the capitals of several countries. Dr. Gutierrez was made honorary member of the urological associations of Colombia, Peru, Chile, Argentina, Uruguay, Brazil and the Venezuelan Surgical Association, the Peruvian Academy of Surgery and the Brazilian College of Surgeons.——Dr. Sidney M. Samis has been appointed assistant director of Mount Sinai Hospital. Dr. Samis, who was a medical corps captain during the war, has served in administrative posts at Montefiore Hospital for Chronic Diseases and the Union Health Center in New York. He is a graduate of St. Louis (Mo.) University Medical School, 1941.——Dr. William Dock, professor of medicine at the Long Island College of Medicine, served as physician in chief pro tempore at the Peter Bent Brigham Hospital, Boston, October 25-30. While there he delivered the E. Stanley Emery Jr. Memorial Lecture on "Peptic Ulcer and Periodic Visceral Pain."

OHIO

Physicians' Fund Aids Medical School.—The Society of General Physicians of Cincinnati established a fund in 1947 for the purpose of making small funds available for the benefit of the University of Cincinnati College of Medicine. The fund is made up of 75 per cent of net proceeds of the postgraduate program of the society. In the past year the following disbursements were made by the dean, who administers the fund: $1,200 for a teaching fellow in the department of obstetrics; $400 for a precision balance for the gastric laboratory and $1,200 to the cardiac laboratory.

Campaign Against Brucellosis.—The Ohio State Medical Association and the State Veterinary Medical Association have initiated a joint campaign to warn farm people of the dangers of brucellosis. The committee on rural health of the state medical association has published a folder which relates the symptoms of brucellosis in man, its menace to human health and steps to be taken to protect the farm family. A companion folder, which gives the latest known facts of diseases among farm animals, is being published by the state veterinary medical association committee on brucellosis. Both folders are to be distributed to farm organizations and county health officials.

TEXAS

Lecture in Neurology.—Dr. Francis C. Grant, professor of neurosurgery, University of Pennsylvania School of Medicine, Philadelphia, will give the James Greenwood Lecture in neurology and neurosurgery at the University of Texas Medical Branch, Galveston, December 6.

University Appointment.—Wiktor W. Nowinski, Ph.D., who has been doing research on enzyme factors in brain metabolism at the University of Texas Medical Branch, Galveston, has been appointed associate professor of neurochemistry.

Sweeney Diabetic Foundation.—This foundation has launched a campaign to raise $100,000 for establishment of a camp for diabetic children and a research laboratory for diabetic and allied research. The camp is to be on 400 acres of land near Gainesville, and the laboratory is to be located in Gainesville. The foundation was organized a year ago by the citizens of Gainesville and named for Dr. J. Shirley Sweeney, who was persuaded to become director of the enterprise. The project has been endorsed by the Cooke County Medical Society.

WASHINGTON

State Medical Election.—At the annual meeting of the Washington State Medical Association in October, Dr. Harold E. Nichols, Seattle, was installed as president. Dr. Donald G. Corbett, Spokane, was chosen president-elect and Dr. James W. Haviland, Seattle, secretary-treasurer. Drs. Ross D. Wright, Tacoma, and Raymond L. Zech, Seattle, were named delegates to the American Medical Association, with Drs. Frank H. Douglass and Vernon W. Spickard, both of Seattle, named as alternates. The next annual convention will be held in Seattle.

GENERAL

Panamerican Convention on Medical Education Postponed.—The secretary of the Panamerican Convention on Medical Education, which was to meet in Lima, Peru, December 3-13, announces that the meeting has been postponed until next year, probably some time in February.

Award to Designer of Lenses.—David S. Grey, Boston designer for lenses for television and receiving sets and microscopes for medical research, received the Adolph Lomb Medal of 1948 at the recent annual meeting of the Optical Society of America in Detroit. As part of his work he has designed new types of microscopic lenses for accurate photography of medical specimens in invisible ultraviolet light.

Tropical Medicine Society Meetings.—The National Malaria Society will meet conjointly with the American Society of Tropical Medicine and the American Society of Parasitologists at the Hotel Roosevelt, New Orleans, December 5-8. The National Malaria Society has scheduled four scientific sessions including a panel discussion on malaria and a joint meeting with the American Society of Parasitologists and the American Society of Tropical Medicine.

Society Election.—At the summer meeting of the American Proctologic Society, the following officers were elected: Harry E. Bacon, Philadelphia, president; Vernon G. Jeurink, Denver, president-elect; Hoyt R. Allen, Little Rock, treasurer, and W. Wendell Green, Toledo, secretary. Since Dr. Jeurink's death July 6, the council has chosen Dr. Louis E. Moon, Omaha, as president-elect.

Conference on Electronic Instrumentation.—A three day conference on the use of electronic instrumentation in the fields of nucleonics and medicine will be held in the Engineering Societies Building, New York, November 29 to December 1, under the auspices of the Institute of Electrical Engineers and the Institute of Radio Engineers. Addresses of the first day will place emphasis on the medical requirements of electronic instruments. A large display of nuclear radiation instruments has been provided by the Atomic Energy Commission.

Impostor Apprehended.—The impostor who was posing as a representative of the American Medical Association for the purpose of inspecting hospital laboratories (THE JOURNAL, October 23, page 602) was apprehended by military police at Fort Hamilton, Brooklyn, early in October and was released to civilian authorities. "Dr. Rumrick" appeared at the Station Hospital, Fort Hamilton. The commanding officer at the hospital, having previously received a telegraphic warning which was sent to U. S. Army hospitals in the New York area, notified the military police. The impostor has pleaded guilty.

Societies Appoint Executive Secretaries.—William C. Stronach has been appointed executive sceretary of the American College of Radiology, which has headquarters in the Civic Opera Building, Chicago, to succeed Mac F. Cahal, who has become executive secretary of the American Academy of General Practice. Mr. Stronach was formerly Mr. Cahal's assistant. Mr. Cahal has been retained as consultant to the American College of Radiology with the title of general counsel. Headquarters of the American Academy of General Practice are located at 231 West 47th Street, Kansas City, Mo.

Dr. Cowgill Receives Nutrition Award.—George R. Cowgill, Ph.D., professor of nutrition at Yale University, received the 1948 Award for Scientific Distinction of the Grocery Manufacturers of America, November 15. The presentation took place during a luncheon at the organization's annual meeting in the Waldorf-Astoria Hotel, New York. Dr. Cowgill was cited for "fundamental contributions to the science of nutrition, particularly his research on the functional role of vitamin B_1, his success as a teacher of young biochemists and his outstanding editorial work for the *Journal of Nutrition*." Each year a committee of the Grocery Manufacturers of America selects for its award a scientist who has made an important contribution to public health in the science of nutrition. Dr. Cowgill, a member of the Yale faculty since 1921, has been a member of the Council on Foods and Nutrition of the American Medical Association since 1938.

Scholarships in Cerebral Palsy.—Scholarships for special study in cerebral palsy are being offered to physicians, therapists and educators by the National Society for Crippled Children and Adults. Funds in the amount of $5,000 per year for three years have been granted to the National Society for this purpose by the Alpha Chi Omega national sorority. The scholarship plan provides for the training of outstanding persons who will be able to assist member societies of the national society in developing, setting up and operating facilities and centers for the use of all public and private agencies interested in helping persons having cerebral palsy. Under the program allotments, varying from $500 to $1,000 for tuition and maintenance at a recognized training center for the minimum of three months, are given to qualified persons. Doctors, therapists, educators and other needed workers are eligible to receive the scholarships. For information address the National Personnel Registry and Employment Exchange, National Society for Crippled Children and Adults, Inc., 11 South La Salle St., Chicago 3.

Staff for WHO Secretariat Appointed.—Since September 1, when the World Health Organization formally became a specialized agency of the United Nations, a number of internationally known public health specialists have been appointed to fill top positions in the World Health Organization Secretariat. Among the persons named by Dr. Brock Chisholm, director-general of the World Health Organization, are the following: Dr. Raymond Gautier, Switzerland, assistant director-general in charge of the department of technical services; Dr. William P. Forrest, United Kingdom, special assistant to the director-general; Dr. Yves Biraud, France, director, division of epidemiology; Dr. William Bonne, Netherlands, director, division of planning; Dr. Frank A. Calderone, United States, director, Technical Liaison Office, New York; Dr. Neville Goodman, United Kingdom, director, Division of Field Operations; Dr. Norman Howard-Jones, United Kingdom, director, Division of Editorial and Reference Services, and Mr. Milton P. Siegel, United States, director of administration and finance.

American Academy of Allergy.—The annual meeting of the American Academy of Allergy will be held at Chalfonte-Haddon Hall, Atlantic City, December 6-8. All physicians interested in allergic problems are invited to attend the sessions as guests of the academy by registering without payment of fee. Included in the program are two memorial lectures to late members of long standing: The first, in memory of Dr. Harry D. Donnally, will be given by Dr. Thomas Francis, Ann Arbor, Mich., on "Immunology of Virus Diseases." The second, in memory of Dr. Robert Ward Lamson, will be given by Drs. Thomas H. Holmes, Helen Goodell, Stewart Wolf and Harold G. Wolff, New York, on "An Experimental Approach to Psychosomatic Phenomena in Rhinitis and Asthma." The presidential address will be made by Dr. Karl D. Figley of Toledo, Ohio. At the banquet December 7 William J. Hale, LL.D., consultant to Dow Chemical Company, Midland, Mich., will speak on "Today's Food and Its Aftermath."

Western Surgical Association Meeting.—The annual meeting of the Western Surgical Association will be held at the Statler Hotel, St. Louis, December 2-4, under the presidency of Dr. Harry B. Zimmerman, St. Paul. Among others the following have been invited to read papers:

Rudolph J. Noer and John W. Derr, Detroit, Revascularization Following Experimental Mesenteric Occlusion.
Arthur C. Pattison, Los Angeles, Portacaval Anastomosis in Cases of Advanced Portal Cirrhosis.
Col. Frank E. Hamilton, M.C., and Major George J. Hayes, M.C., Washington, D. C., Pre-Frontal Lobotomy in the Management of Intractable Pain.
Stanley E. Lawton and Arthur R. Marks, Chicago, Gastrojejunocolic Fistula.
E. Lee Strohl and Guy V. Pontius, Chicago, Multiple Polyposis of the Colon.
Charles W. Mayo and Roberta G. Rice, Rochester, Minn., Situs Inversus Totalis: Statistical Review of 76 Cases with Special Reference to Disease of the Biliary Tract.
Frederick R. Harper, William B. Condon and William H. Wierman, Denver, Chronic Suppurative Lung Disease.
Ralph G. Carothers, Cincinnati, and Foster J. Boyd Jr., Indianapolis, Traction Technique for the Reduction of Colles' Fractures.
Robert A. Wise, Portland, Ore., Hemipelvectomy for Malignant Tumors of the Bony Pelvis.

The presidential address will be delivered at the opening of the Friday afternoon session. The annual dinner will be December 3 at 6:30 p. m.

Pharmaceutical Manufacturers Award.—The National Institutes of Health, Bethesda, Md., have been selected to receive the American Pharmaceutical Manufacturers' Association 1948 Scientific Award. It will be presented by Dr. Ernest E. Irons, Chicago, President-Elect of the American Medical Association, at a dinner in the Waldorf-Astoria Hotel, New York, at 8 p. m., December 7. Dr. Rolla E. Dyer, director of the institutes, will give the acceptance address. The ceremony attending the award will consist of morning, afternoon and evening sessions reporting new and basic information on major research progress in drug therapy. The program is as follows:

Austin Smith, Chicago, Trends in Drug Therapy Research.
Cornelius P. Rhoads, New York, Basic Research Progress in the Field of Cancer.
Milton V. Veldee, Washington, D. C., Trends in the Field of Biologic Products.
Perrin H. Long, Baltimore, Basic Research Progress in the Field of Antibiotics.
Keith S. Grimson, Durham, N. C., Basic Research Progress in the Field of High Blood Pressure.
Randolph West, New York, Use of Vitamin B_{12} in Treatment of Pernicious Anemia.
Isaac Starr, Philadelphia, On the Stimulation of Medical Research by Means of Grants: Its Promise and Its Dangers.
Charles G. King, Ph.D., Scarsdale, N. Y., Basic Research Progress in the Field of Nutrition.
Roy R. Kracke, Birmingham, Ala., Basic Research Progress in the Field of Blood Disorders.
Arthur C. DeGraff, New York, Basic Research Progress in the Field of Heart Diseases.
Charles Ragan, New York, Basic Research Progress in the Field of Arthritis.
Howard T. Behrman, New York, Basic Research Progress in the Field of Dermatologic Disorders.

In the past four years this award has been given to the National Research Council, the Rockefeller Institute for Medical Research and the American Medical Association.

Social Hygiene and the Defense Program.—The American Social Hygiene Association has reactivated its Committee on National Defense Activities, and preliminary conferences have been held with representatives of the National Defense Establishment and United States Public Health Service. The Interdepartmental Venereal Disease Control Committee, which was appointed during World War II and comprises representatives of the Army, Navy, Air Force, National Defense Establishment as such, the U. S. Public Health Service, the Federal Security Agency, and the American Social Hygiene Association as an advisory member, also held a conference and formulated proposals for the services of the association to be included in the Defense Program. Among the proposals submitted to the president of the association were: to act as an advisor to the National Defense Establishment in matters pertaining to community education and the repression of prostitution; to make available to the armed forces, on request, educational material and advisory services; to bring citizen support to good law enforcement, social treatment and individual health education through the home, the church and the school.

A grant from the reserve funds of the United Service Organization enables the American Social Hygiene Association to undertake the services requested by the interdepartmental committee. The staff has already been recruited, trained and assigned to field and headquarters duties. Field offices have been established where required, and close cooperation with military authorities has been established on national, regional and local levels.

Among the objectives of the new project are to provide military and civilian authorities with reliable information concerning demoralizing conditions which may result in the spread of venereal diseases, especially near military posts and defense industrial establishments; to interpret to the public the present character guidance policy of the National Defense Establishment as it relates to the men and women in these services.

Dr. Walter Clarke, executive director of the American Social Hygiene Association, has general supervision of the project from the main office at 1790 Broadway, New York. This project will be kept separate from the permanent activities of the American Social Hygiene Association, which are financed entirely by private gifts through the Community Chest and sponsored appeals, and which will go along as usual.

Marriages

WILLIAM CUNNINGHAM CRITTENDEN, Birmingham, Ala., to Miss Constance C. Glasgow of Lexington, Va., in August.

ABRAHAM IRVING FRIEDMAN, Hackensack, N. J., to Miss Helene Marion Bennett of New York, in August.

HUGH FRANKLIN SWINGLE JR., Johnson City, Tenn., to Miss Joan Dickey Lincoln of Marion, Va., August 21.

JOSEPH A. AMBROSINO, New York, to Miss Roberta Ann Redden of Dover, N. H., in August.

HARVEY JAMES HOWARD, St. Louis, to Mrs. Alice Tilson Eastes of Baltimore, August 24.

ALIZA COLE, Chilhowie, Va., to Mr. Robert A. Lightburn at New York, August 1.

Deaths

James King Hall ✦ Richmond, Va.; born in Piedmont, N. C., Sept. 28, 1875; Jefferson Medical College of Philadelphia, 1904; member of the National Committee on Mental Hygiene, American Association on Mental Deficiency, Association for the Study of Internal Secretions, American Association for the Advancement of Science and the Virginia Academy of Science; past president of the American Psychiatric Association, Association of Private Psychiatric Hospitals, Richmond Academy of Medicine, Tri-State Medical Association of Virginia and the Carolinas and the Southern Psychiatric Association; in 1933-1934 vice president of the Medical Society of Virginia; specialist certified by the American Board of Psychiatry and Neurology; served as member of the board of the Central State Hospital, Petersburg, and chairman of the Governor's Board on Criminal Mental Hygiene; for many years member of the medical staff of the State Hospital, Morganton, N. C., one of the founders and medical superintendent of the Westbrook Sanatorium; associate editor of *Southern Medicine and Surgery* and *Diseases of the Nervous System*; in 1935 received the honorary degree of LL.D. from the University of North Carolina; died September 10, aged 73.

Francis Parkman Denny ✦ Brookline, Mass.; born in Brookline, Mass., Jan. 2, 1869; Harvard Medical School, Boston, 1895; at one time on the faculty of his alma mater; for many years health officer; established a bacteriologic laboratory in the city in 1899, the first in Massachusetts outside Boston, a tuberculosis pavilion as part of the Brookline contagious disease hospital in 1914 and a dental dispensary in 1915; member of the New England Pediatric Society and of the American Public Health Association; member of the executive committee and honorary vice president of the Massachusetts Tuberculosis League; past president of the Massachusetts Public Health Association, the Norfolk District Medical Society and the Brookline Anti-Tuberculosis Society; for twenty-six years responsible for the quarterly publication of the *Brookline Health Bulletin;* during his term of office as health officer Brookline was three times the winner of a health conservation contest sponsored by the United States Chamber of Commerce; died in New London, N. H., September 6, aged 79.

Paul Scott Hansen, Santa Barbara, Calif.; born in Columbus, Ohio, Oct. 16, 1910; Northwestern University Medical School, Chicago, 1938; interned at St. Luke's Hospital in Chicago and Massachusetts General Hospital in Boston; member of the American Medical Association; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; formerly on the faculty of the University of Pennsylvania School of Medicine in Philadelphia and the Yale University School of Medicine, New Haven; served as a captain with the 15th Evacuation Hospital in Africa, Sicily and Italy; separated from the service as a major after thirty-three months of service overseas; consultant on blood diseases at the Santa Barbara Clinic; affiliated with the Santa Barbara Cottage Hospital and the Santa Barbara General Hospital, where he died September 26, aged 37, of poliomyelitis.

Bert Ira Beverly ✦ Oak Park, Ill.; born in Richfield, Ohio, June 2, 1894; Rush Medical College, Chicago, 1924; clinical associate professor of pediatrics (Rush) at the University of Illinois College of Medicine, Chicago; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics, serving for many years as chairman of the mental health committee; member of the Illinois State Commission for Handicapped Children; served during World War I; head of the behavior clinic at the Central Free Dispensary, Presbyterian Hospital; consultant psychiatrist at the Shriners Hospital for Crippled Children and for many years on the staff of Children's Memorial Hospital, all in Chicago; author of "In Defense of Children" and "A Psychology of Growth"; died September 27, aged 54, of rupture of the chordae tendinae.

Edwin Welles Kellogg, New York; born in 1878; New York Homeopathic Medical College and Hospital, New York, 1903; member of the American Medical Association; fellow of the American College of Surgeons; formerly on the faculty of his alma mater; an officer during World War I; served as a member of the medical practice committee which had jurisdiction over all physicians and surgeons practicing in workmen's compensation cases in New York; consulting surgeon, New York Ophthalmic Hospital; affiliated with the Doctors, Park East and Flower and Fifth Avenue hospitals; died in Washington, Conn., September 11, aged 69.

Fritz Carleton Hyde, New York; born in Grand Rapids, Mich., June 3, 1876; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; at one time president of the Connecticut Medical Examining Board; member of the New England Surgical Society; fellow of the American College of Surgeons; served during World War I; for many years chief of staff and chief of medical service at the Greenwich (Conn.) Hospital and consulting surgeon at the Cape Cod Hospital in Hyannis, Mass.; died in Harwichport, Mass., September 4, aged 71, of arteriosclerosis and hemiplegia.

Joseph Francis Bredeck ✦ St. Louis; born in St. Louis, in 1890; Washington University School of Medicine, St. Louis, 1914; received the doctor of public health degree from the University of Pennsylvania in 1917; since 1933 health commissioner; instructor in clinical medicine and lecturer in public health at his alma mater; served in France during World War I; fellow of the American College of Physicians; a drive for funds to establish a public health scholarship in his honor is being organized by friends and associates; died October 4, aged 58, of heart disease.

Robert Meston Bolton, Durham, N. H.; born in Somerset, Md., May 19, 1903; George Washington University School of Medicine, Washington, D. C., 1931; member of the American Medical Association and the Medical Society of the District of Columbia; served in the medical corps of the U. S. Naval Reserve during World War II; formerly on the staffs of the Garfield, Children's, Columbia, Casualty and Doctors hospitals in Washington, D. C.; recently appointed director of the health service at the University of New Hampshire; died September 16, aged 45.

Ward Ariel Anderson, Portland, Ore.; Ohio Medical University, Columbus, 1906; on the staff of Morningside Hospital; died in Emanuel Hospital August 24, aged 71, of heart disease.

Cecil V. Bachelle ✦ Chicago; Rush Medical College, Chicago, 1900; fellow of the American College of Surgeons; formerly on the faculty of the College of Physicians and Surgeons, School of Medicine of the University of Illinois; affiliated with Walworth County Hospital in Elkhorn, Wis., and Henrotin Hospital; died September 21, aged 73, of chronic myocarditis.

George Elliott Patrick Barnes, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1931; member of the American Medical Association; served during World War II; affiliated with Southern Baptist, Lakeshore and Mercy hospitals; died September 4, aged 43, of injuries received in an automobile accident.

Ben P. Bell, Oklahoma City; University of Oklahoma School of Medicine, Oklahoma City, 1942; member of the American Medical Association; interned at St. John's Hospital in Tulsa; served a residency at St. Elizabeths Hospital in Washington, D. C.; served in the medical corps of the U. S. Naval Reserve during World War II; affiliated with the Coyne Campbell Sanitarium; killed September 5, aged 33, when the plane he was flying crashed.

Clarence Joseph Bertaut, Chicago; St. Louis College of Physicians and Surgeons, 1920; Chicago Medical School, 1922; on the staff of the Bethany Hospital; died in Oak Park, Ill., September 14, aged 52, of coronary thrombosis.

Newton Emerson Bitzer ✦ Lancaster, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; fellow of the American College of Surgeons; examiner for the draft board during World War I; served as a member of the local board of health; for many years medical director of St. Joseph's Hospital; died in Lancaster General Hospital August 15, aged 75.

Bert John Bixby, Buffalo; University of Buffalo School of Medicine, 1903; member of the American Medical Association and the National Gastroenterological Association; veteran of the Spanish-American War and World War I; served on the staff of the Millard Fillmore Hospital; died September 7, aged 72, of hypertrophic cirrhosis of the liver.

Nathan Bernard Bluestone ✦ Yorktown Heights, N. Y.; University of Glasgow Medical Faculty, Scotland, 1933; member of the board of education; on the staffs of the Peekskill (N. Y.) Hospital and Northern Westchester Hospital in Mount Kisco; served overseas during World War II; died August 25, aged 43.

Peter Bourbaki, Kansas City, Kan.; National University of Athens School of Medicine, Greece, 1895; Loyola University School of Medicine, Chicago, 1917; served on the staffs of Bethany Hospital, Providence Hospital and St. Margaret's Hospital, where he died September 8, aged 75, of multiple myeloma.

Walter R. Brock ✠ Sheldon, Iowa; Drake University Medical Department, Des Moines, 1894; past president of the Sioux Valley Medical Association, serving for many years as treasurer; in 1931 vice president of the Iowa State Medical Society; past president of the O'Brien County Medical Society; for many years city health officer; on the staff of Good Samaritan Hospital; died September 11, aged 78, of coronary occlusion.

Henry Alexander Brown, Los Altos, Calif.; Medico-Chirurgical College of Philadelphia, 1900; member of the American Medical Association; veteran of the Spanish-American War; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology; formerly on the staff of the Stanford University School of Medicine, San Francisco; died September 18, aged 77, of coronary disease.

James Mack Brown, Gadsden, Ala.; Medical College of Alabama, Mobile, 1889; member of the American Medical Association; died August 14, aged 82, of coronary thrombosis.

Richard C. Buchanan ✠ Green Bay, Wis.; Detroit College of Medicine, 1896; fellow of the American College of Surgeons; on the staffs of St. Mary's Hospital, Bellin Memorial Hospital and St. Vincent's Hospital, where he died August 21, aged 78, of coronary thrombosis.

Charles Howard Cale, Neffs, Ohio; Starling Medical College, Columbus, 1904; member of the American Medical Association; past president of the Belmont County Medical Society; affiliated with City Hospital in Bellaire; died July 23, aged 72, of acute coronary occlusion.

William R. Camp, Fairburn, Ga.; Atlanta Medical College, 1890; member of the American Medical Association; formerly mayor and for many years on the city council; county physician; died August 25, aged 80, of carcinoma of the lung.

Thomas Francis Capeles ✠ Haverhill, Mass.; Tufts College Medical School, Boston, 1909; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the New England Otological and Laryngological Society; affiliated with the Massachusetts Eye and Ear Infirmary, Boston, and Hale Hospital; member and clerk of the Haverhill park board; died August 12, aged 63, of uremia and carcinoma of the prostate.

Webb Parks Chamberlain ✠ Cleveland; Western Reserve University Medical Department, Cleveland, 1903; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Ophthalmology; affiliated with the Lakewood and Lutheran hospital; died July 20, aged 71, of carcinoma.

Helen E. Collins, Chicago; Hering Medical College, Chicago, 1900; died September 26, aged 78, of pneumonia.

Willis Scott Cooke, Cazenovia, N. Y.; New York University Medical College, New York, 1897; formerly member of the state compensation board; served during World War I; died in the Crouse Irving Hospital, Syracuse, September 2, aged 75, of coronary thrombosis.

Charles Campbell DeKlyn, New Rochelle, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1905; served during World War I; on the consulting staff of the New Rochelle (N. Y.) Hospital, where he died September 7, aged 66.

Lillian Elizabeth Dempsey, Vallejo, Calif.; University of Oregon Medical School, Portland, 1896; died September 19, aged 75, of cerebral hemorrhage.

Michael F. J. Donovan ✠ Chicago; Bennett Medical College, Chicago, 1915; surgeon for the Chicago, Rock Island and Pacific Railroad; affiliated with St. George Hospital, where he died September 17, aged 65, of coronary thrombosis and diabetes mellitus.

James Maurice Downey ✠ Brooklyn; Long Island College Hospital, Brooklyn, 1891; also a graduate in pharmacy; fellow of the American College of Surgeons; past president of the Brooklyn Surgical Society; affiliated with the Hospital of the Holy Family and St. Mary's Hospital; died September 12, aged 82, of coronary disease.

Sylvester Amos Draper, Orlando, Fla.; Medical College of Virginia, Richmond, 1900; died August 16, aged 74.

Robert Earl, St. Paul; University of Minnesota College of Medicine and Surgery, Minneapolis, 1896; member of the American Medical Association and the Western Surgical Association; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; affiliated with the Midway and Mounds Park hospitals; died August 11, aged 65.

Gottfried Arthur Estel ✠ North Madison, Ind.; St. Louis University School of Medicine, 1904; affiliated with the Madison State Hospital; died in Murphysboro, Ill., August 20, aged 68, of chronic endocarditis.

Marvin A. Gantt, Houston, Texas; Louisville (Ky.) Medical College, 1904; member of the American Medical Association; died recently, aged 70, of carcinoma of the liver.

William Harris Gitman, Dayton, Ohio; Université de Lausanne Faculté de Médecine, Switzerland, 1938; member of the American Medical Association; interned at the Good Samaritan Hospital; served during World War II; affiliated with the Good Samaritan, Miami Valley and St. Elizabeth hospitals; died September 3, aged 40, of coronary thrombosis.

William Christian Hager, Brooklyn; Long Island College Hospital, Brooklyn, 1896; visiting physician at the Swedish Hospital; died September 12, aged 81, of uremia.

Henry Steers Holland, New York; Columbia University College of Physicians and Surgeons, New York, 1905; member of the American Medical Association; fellow of the American Society of Anesthetists; on the staff of Sloane Hospital for Women and the Doctors Hospital; died in the Midtown Hospital August 28, aged 67, of carcinoma of the left submaxillary gland.

Otto Landman, Toledo, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1887; fellow of the American College of Surgeons; on the staff of St. Vincent's Hospital; died July 11, aged 86, of Parkinson's disease.

Ross Simonton McElwee ✠ Statesville, N. C.; University of Maryland School of Medicine, Baltimore, 1909; member of the House of Delegates of the American Medical Association from 1941 to 1945; member of the Radiological Society of North America; on the staff of the H. F. Long Hospital; president of the Statesville Chair Company and the Statesville Industrial Bank; died September 8, aged 68, of carcinoma.

DIED WHILE IN MILITARY SERVICE

Jack Leslie Doughtie ✠ Lieutenant Colonel, M.C., U. S. Army, Cleburne, Texas; born in Cleburne, Sept. 26, 1912; University of Texas School of Medicine, Galveston, 1937; formerly an intern at the John Sealy Hospital in Galveston and a resident at the Brackenridge Hospital in Austin; entered the medical reserve corps of the U. S. Army in July 1940 and served until July 1941, when he entered the regular army; served a residency at the Brooke General Hospital, Fort Sam Houston, San Antonio; died in the Walter Reed General Hospital, Washington, D. C., March 22, aged 35, of heart disease.

William Wills Green Jr., Tarboro, N. C.; Duke University School of Medicine, Durham, 1944; interned at the Duke Hospital in Durham; certified by the National Board of Medical Examiners; member of the American Medical Association; captain, medical corps, Army of the United States; died March 18, 1947, aged 26, of cerebral hemorrhage.

Albert Clark Kinney Jr., Hardwick, Vt.; University of Vermont College of Medicine, Burlington, 1946; interned at the Maine General Hospital in Portland, Me.; first lieutenant, medical corps, Army of the United States; killed in Alaska Dec. 28, 1947, aged 27, while on a mission to rescue the crew of an airplane which crashed on the Seward Peninsula.

Edward George Meter Jr., Merion Station, Pa.; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1936; interned at the Fitzgerald-Mercy Hospital in Darby, Pa., served a resident fellowship in radiology at the Graduate Hospital of the University of Pennsylvania in Philadelphia; specialist certified by the American Board of Radiology; major, medical corps, Army of the United States; attached to the 183rd General Hospital, Fort Richardson, Alaska; died June 12, 1947, aged 38, of acute myocardial infarction.

Maurice Louis Silverstein, Boston; Boston University School of Medicine, 1923; member of the American Medical Association; interned at the Massachusetts Homeopathic Hospital; commissioned a captain in the medical corps, Army of the United States, Feb. 4, 1944; died in the Lovell General Hospital, Fort Devens, Mass., Feb. 16, 1946, aged 47, of tuberculous meningitis.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 23, 1948.

The Remuneration of Specialists in the National Health Service

A body known as the Spens Committee was recently appointed by the government to investigate and report on the remuneration of specialists employed under the National Health Service. They recommended that the total range of remuneration for a full time specialist should be $6,000 to $20,000, but that remuneration above $10,000 should depend on the award of special distinction. The government now announces that it has had under review the report of the Spens Committee and has decided to set up a special awards committee. It will be a national committee charged to select those specialists whose outstanding distinction merits higher financial rewards than the normal rates.

The principle of the decision cannot be gainsaid, but how is it likely to work? It is certainly a delicate operation, which is entirely new in this country, for a committee to make a survey of the specialists of the country and decide who are to be proclaimed "distinguished" and who not. Another trouble is the matter of expense, but that never seems to trouble the socialist government, who have made permanent, as far as they can, the crushing taxation of the war. As the consultations with or treatment by specialists are free to the patients, they will demand the specialists who have been dubbed "distinguished" to the neglect of the others. It is well known that many of the younger men, who are to get lower remuneration, are just as competent for many purposes as the "distinguished" ones. Under private practice the matter is easily solved. The general practitioner recommends the specialist most suitable both for the case and the patient's pocket. But under National Health Insurance he passes the unnecessary increased cost on to the taxpayer.

The Nuffield Foundation

The Nuffield Foundation, because of the munificence of the automobile magnate Lord Nuffield, has spent or promoted grants amounting to $8,500,000 for research in its first five years. In their third report, just published, the trustees welcome the increased support of the state for learning and research but think that this does not decrease the need of alternate sources of support if the democratic principle is to be upheld, that there should be room for more than one opinion and for more than one means of putting that opinion to the test. The foundation is supporting three university chairs of industrial health, one of child health and four schools of dentistry. It is also financing laboratory studies of the blood and of the physiology of learning in animals, as well as some important sociomedical inquiries. A remarkable one is into the nature and circumstances of the middle class, "the main repository not only of administrative and professional ability but also of our cultural capital." This class has in the past received far less attention than have the wage earners. The work is to be undertaken by the London School of Economics with a view to studying not only how people rise and fall in our complicated caste system but also whether the prevailing conditions of life for the middle class are becoming too difficult. The difficulty certainly is mainly due to the confiscatory prolongation of taxation on the war level to finance the socialistic measures of the labor government.

A gift of $1,800,000 has been made to the Nuffield Foundation by Captain O. Bird, who has suffered from osteoarthritis for many years, for promotion of research into the prevention and cure of rheumatism.

Rehabilitation Centers

Since the war great attention has been given to rehabilitation. It began with the treatment of those who had recovered from their wounds but has been extended to disability due to other causes. For several years a residential rehabilitation center for the reconditioning of men who have left a hospital but are not fit immediately for full time employment or vocational training has been in operation near London, at Egham, Surrey. The experiment has so justified itself that the Ministry of Labor began to make plans for other centers, but there is great difficulty in securing premises and adapting them for this purpose. The Minister of Labor has therefore decided to use government training centers temporarily.

The objects of the course at these centers are as follows: (1) to restore to fitness and confidence those who, although not in need of active medical treatment, are not fit for full time employment; (2) to discover by observation and tests and with medical advice the personal factors impeding satisfactory settlement in employment and the types of employment most likely to lead to permanent resettlement and (3) to give guidance to placement officers of the Ministry about the effects of a disability on a person's working capacity. The maximum length of the course will be twelve weeks, but it is expected that in the majority of cases a month or six weeks will be sufficient. Efforts will be made to find for the person the type of employment or training recommended by the specialist officers. Those undergoing the course will receive allowances for their support. Three centers have already been opened, and it is planned to open ten more in large towns.

What is an Accident?

What is an accident may seem to be a simple question to most persons, but the lawyers wrangle about the meaning of the term. The medicolegal correspondent of the *British Medical Journal* points out that the tendency of our highest tribunal, the House of Lords, to interpret the Workmen's Compensation Acts "beneficially" has led to decisions which have expanded the concept of injury by accident to an extent that puts a severe strain on the sense of the ordinary person. Compensation was awarded to a workman who claimed that he contracted Raynaud's disease from vibration of a rotary tool and to another who suffered from hernia alleged to be due to vibration of a pneumatic drill. The classic case, on which these decisions were based, was that of a girl who, after sustaining numerous cuts and scratches on her hands in the course of her work over a long period, became totally incapacitated as a result of blood poisoning. It was held that she was not the less entitled to compensation because her disease was due not to one definite and specified accident but to a series of accidents, each of which was specific and ascertainable, though its actual influence on the resulting illness could not be precisely fixed. But at last the House of Lords seems to have called a halt to this process of extension of the meaning of accident.

A workman contracted silicosis through prolonged work as a slate cutter. He complained compensation for injury by accident, arguing, as in the previous cases, that each particle of silica had caused a separate accident and that his condition was due to accumulation of these slight injuries. His claim was rejected on the grounds that the disease was not due to an accident as the word was used in the Act, or to a series of accidents, but was the result of a continuing process repeated from day to day. Although it is possible to analyze silicosis into a series of separate injuries caused by separate accidents, the attribution of the disease to an accidental cause is unreal. The distinction between accident and disease is well founded. No explicit formula could be adopted with safety, but there must come a time when the indefinite number of so-called acci-

dents and the length of time over which they occurred take away the element of accident and substitute that of process. Silicosis is such and could not be said to be the result of injury by accident. The case of the girl with the scratched hands was the high water mark of cumulative injury by infinitesimal accidents.

PARIS

(From Our Regular Correspondent)

Oct. 21, 1948.

Neurosyphilis and Penicillin

Girard, Moreau and H. Fraisse have reported to the Lyons Society of Dermatology and Syphilography their results in 19 cases of neurosyphilis treated with intramuscular injections of penicillin every three hours, or twice a day in a delaying substance. They began treatment with a dose of 30,000 units and progressed up to 300,000 units, to a total of 5,000,000 units. In tabes, results were on the whole satisfactory: fulgurating pains disappeared frequently, even in cases that had resisted all previous treatments; improvement of sphincter disorders occurred, and there was the possibility of an improvement of ataxia. In general paralysis, results were less brilliant; rather frequently, however, there was improvement of disorders affecting intellect and character, and a disappearance, after treatment, of hyperalbuminosis and hypercytosis in the cerebrospinal fluid. The serologic reaction remained positive most of the time. In dementia paralytica penicillin is to be considered rather as an adjuvant, associated with malaria therapy. The authors have noted a few reactions consisting in the aggravation of functional signs and, in 1 case, in the transitory appearance of Wernicke's aphasia, which proves that the treatment has to be used cautiously.

New Laws Concerning Venereal Disease

The new law of July 8, 1948, grants to sanitary authorities the right to demand from a person against whom exist "precise, serious and concordant presumptions" of having contaminated one or several persons with a venereal disease a medical certificate stating whether he has a contagious venereal disease or not. If this certificate seems contradictory to the epidemiologic history, a medical examination by an approved venereologist or an approved dispensary can be demanded. The new law reinforces the compulsory sanitary supervision, decreed in 1947, of every person entered in the sanitary and social registry of prostitutes. The sanitary authority is to be informed of any change of residence of any person placed under sanitary supervision, and all prosecutions for soliciting have to be reported to the Sanitary Authority in order to enable it to cause the said person to be examined. The notation in the registry of prostitutes now becomes compulsory when there is repetition of the offense or when the person suffers from a venereal disease. But the same section prohibits the inclusion in the registry of any defaulter under 18 years of age and of any under 21 on probation. Another law, of Aug. 28, 1948, divides the antivenereal dispensaries into three categories: (1) public dispensaries run by the state, (2) those run by associations recognized as of public interest and by institutions of the Social Security and (3) dispensaries run by private organizations and private persons; these can be open only after a previous agreement of the "Préfet," granted on recommendation of the district health director. Every department must have at least one hospital comprising a ward for venereal diseases. In every department, the service of the antivenereal campaign is to be under the management of a doctor in chief, appointed by the Ministry for Public Health and Population. The state shares the expense of establishing new dispensaries and for the extension of old ones. The subsidy may reach 50 per cent of the cost.

Death of Professor Lenormant

Professor C. Lenormant died at the age of 73. A descendant of intellectual ancestors, he was a brillant scholar and a disciple of Reclus, Bouilly, Gerard, Berger, Marchant and Rochard. He was a hospital surgeon at the age of 27, associate professor at the age of 30 and professor of surgical clinics at the age of 43. His works on encapsulating plastic peritonitis, volvulus of the cecum, rectal prolapse, diaphragmatic hernias, traumatic chylothorax, thymus hypertrophy and fractures of the calcaneus will long retain their value in the history of surgery. In collaboration with P. Lecene, whom he succeeded in the professorship of external pathology, he studied hemorrhagic pancreatitis, pneumococcic peritonitis, exostoses and chondromas and nonparasitic cysts of the long bones. He had been, for a time, general secretary to the Academy of Surgery. He contributed to the *Presse Médicale* and the *Journal de Chirurgie*, of which he was one of the founders. During the occupation he was a *resistant*; on his proposal, the Academy of Medicine voted a protest against the gynecologic visit, imposed on French women deported to Germany by the "Service of Compulsory Labor." It was he who wrecked the Nazi scheme to pair each of the principal French medical journals with a German review.

BRAZIL

(From Our Regular Correspondent)

SÃO PAULO, Oct. 25, 1948.

Amebiasis and Chronic Cholecystitis

In 500 cases of intestinal amebiasis, Professor Felicio Cintra do Prado of Escola Paulista de Medicina found 11 cases in which there was a prevalence of symptoms generally attributed to disturbances of the biliary ducts. The patients showed steady or intermittent pain in the hepatic region, tenderness over the vesicular area, nausea before breakfast and dyspeptic pain caused by foods, especially fatty foods. Cholecystography and duodenal intubation did not reveal any abnormality in these patients; feces, however, contained Endameba histolytica, and the apparently vesicular symptoms disappeared with the specific antiamebic treatment. Such cases are due to general toxic manifestations acting sporadically on the vesicular functions and, perhaps, in some cases to colitis predominating on the hepatic flexure, according to Professor Prado.

Nervous Reactions to Diphenhydramine Hydrochloride

Dr. J. Pereira Jr. of Instituto Biologico of São Paulo reported recently the case of a white man aged 23 years who, after 300 mg. of diphenhydramine hydrochloride, taken over a period of three days, had from the fourth day on tendency to sneeze and a dysenteric syndrome of short duration with nausea and vomiting; on the fifth day, somnolence, confusion, hallucinations and purposeless kinetic impulses; a sallow skin; bilateral palpebral drop with temporary blindness; internal strabismus of the right eye with paralytic bilateral mydriasis; he was always apyretic and without convulsions or spasticity; deep and cutaneous reflexes were decidedly depressed, but pulse rate, blood pressure and temperature were always in normal range. In four days all signs, but the ocular, were on the wane. The latter disappeared slowly in about one and a half months, with residual hemianopsia of the left eye.

After comparison of the side and toxic effects of the drug, in the literature and in this case, with signs of local bulbar anesthesia in animals, the theory is put forward that the narcotic effects and permeability-changing properties of the drug with respect to the nervous system explain the symptoms noted, without regard to any local atropine-like action of the drug.

Correspondence

UNIVERSIDAD CATOLICA DE CHILE ESCUELA DE MEDICINA

To the Editor:—In the May Issue of THE JOURNAL an article was published on Medical Education in Latin America, by Dr. Morris Fishbein. In the paragraph devoted to Chile, he made several observations on the official medical school, which is supported by the government. With regard to our Catholic University school of Medicine, he merely names it to state that it is controlled by the official school, that it follows the French system of teaching and that it has only five years of medical studies.

In order to add some information to that already given, we wish to inform you of several facts which may be of interest.

1. The Catholic University School of Medicine has been in existence only eighteen years. It has gradually increased its courses as far as the fifth year, thus excluding only the medical specialties, because it lacks the necessary hospital facilities.

2. The admittance to the first year of premedical studies is limited to only forty students, every year selected from about two hundred applicants. A second selection takes place during this year, as only thirty are admitted to the final examination.

3. The premedical teaching, which correspond to the first two and one-half years, is principally practical, given in the different laboratories, which are properly and sufficiently equipped for the number of pupils to be trained there.

4. The medical teaching, initiated in the second half of the third year, is given in the clinical hospital, provided with one hundred and fifty beds and adequate services of a clinical laboratory, a roentgenologic laboratory and a laboratory of pathologic anatomy. The medical teaching is also fundamentally practical, and the students have to spend four hours each morning in the hospital wards, medical and surgical on alternate days, and in the afternoon, besides attending some other courses of the curriculum, they assist in the outpatient department and make rounds in the wards assigned to them.

The medical and surgical teaching is not divided into secondary courses, but is fundamentally unified.

5. There are two medical libraries, one medical in the hospital, and one premedical in the medical school. About seventy medical publications are regularly received, but the number of books available is small because of scarcity of funds.

6. The research work that is done in the different laboratories is indicated by the fact that during the last six years they have produced scientific papers, published in known North American, European and Chilean medical magazines. (We are sending a list of these papers).

7. With regard to the teaching staff, about 80 per cent are half time workers in the medical school or hospital, and 5 per cent are in full time jobs. We recognize that this is a considerable handicap and that all of these men receive insufficient salaries, but our scarcity of funds does not allow us to do better.

Finally, we want to make it clear that this type of medical teaching follows much more closely on the North American system than the French or Spanish plan, and it has been successfully applied because many of our head men have had a medical or a scientific training in different North American medical schools and hospital or scientific centers, and because some of our laboratories have benefited from funds given by North American foundations for the development of scientific research.

JOAQUIN LUCO, M.D.,
Director of the Medical School.
The Medical Department,
Catholic University of Chile.
RAMON ORTUZAR, M.D.,

CLUBFOOT IN NEWBORN INFANTS

To the Editor:—I am writing you in reference to the article in the September 4 issue of THE JOURNAL, page 19, "Cohesive Bandage for Clubfoot in Newborn Infants," by Emil D. W. Hauser, M.D., Chicago. I think it extremely unfortunate that an orthopedic surgeon with the standing of Dr. Hauser, particularly one who is so well recognized for his knowledge and skill in treatments of condition of the foot, would make such positive and misleading statements in regard to the use of plaster in the treatment of congenital clubfeet.

Whether or not plaster is the best method, or whether or not cohesive bandage is an improvement over the plaster technic, it has been well established for many years that plaster of paris casts could be applied as early as the first day with perfect safety and that correction could and should be promptly started. I think it is unfortunate that in a journal which is primarily directed toward the general practitioner statements should be made that it has been the practice to postpone the treatment of congenital clubfeet until the infant is 3 months old because of difficulties in plaster technic. Whether one uses adhesive plaster, plaster of paris, Dennis-Brown splints or cohesive plaster, it has been the practice for many years among orthopedic surgeons to start treatment within the first few days after birth.

In Dr. Hauser's desire to emphasize the improvement by the use of cohesive bandage, I am afraid he has been guilty of overstatement in regard to the difficulties and dangers of other methods.

We have been teaching our students for many years of the importance and necessity of treating these cases immediately after birth, and it seems unfortunate that the implication should be made that unless they are treated by cohesive bandage, treatment must be postponed for three months.

DON H. O'DONOGHUE, M.D., Chairman,
Department of Orthopedic Surgery,
University of Oklahoma School of Medicine.

To the Editor:—The article by Emil Hauser in THE JOURNAL for September 4, page 19, undoubtedly must have been read with considerable astonishment by many orthopedic surgeons.

It contains statements which most of us have not found to be true in our practice. ". . . plaster technic is extremely difficult and generally considered impossible until the infant is 3 months old. . . ." I do not know just how many newborn infants with clubfoot have been corrected by myself before they even left the nursery of the obstetrical department, but the number is considerable. ". . . it was impossible to treat newborn infants because of technical difficulties. . . ." This is a most amazing statement, and I am sure that it has amazed other orthopedic surgeons also. Personally, I have never encountered any particular difficulties in applying small plaster bandages to the tiny feet of newborn infants.

It is unfortunate that the magazine *Newsweek* picked up the article and published it, since it creates an entirely wrong impression, not unlike the articles of one rather prominent scribbler of medical potboilers.

One calls to mind the remark made by Frank Ober when one of my fellow students long ago asked him how long one should wait before beginning to correct a clubfoot. His reply was: "If it is a breech, you wait until the head's delivered."

EDWARD PARNALL, M.D.
Albuquerque, N. M.

NOTE:—These letters were referred to Dr. Hauser, who writes:

To the Editor:—We are all in accord with the statement at the outset of the article, that the sooner clubfoot is treated the better. Apparently, however, our experience and observation have led to different conclusions as to the feasibility of using and maintaining plaster casts on newborn infants and up to the age of

3 months. It was because I encountered and observed difficulties in applying such casts, keeping them in place and removing them, that I felt special gratification in developing the treatment with the cohesive bandage and in sharing the results with others in the profession.

EMIL D. W. HAUSER, M.D., Chicago.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Lead Poisoning as Probable or Possible Cause of Death.—This was a petition for a workmen's compensation award for the death of an employee. From the granting of an award to the widow, the insurance company appealed to the district court of appeal, first district, division 2, California.

The employee was a lead burner, and, although the primary cause of death was fibrinopurulent meningitis, an autopsy disclosed an abnormal amount of lead stored in his bones, brain and kidneys. Fibrinopurulent meningitis is a disease caused by a variety of organisms, some more virulent than others, and it was impossible in this case to determine the organism involved because the employee's body had been embalmed before the autopsy was performed.

The medical testimony disclosed a conflict as to whether the meningitis or lead poisoning caused the death of the employee, and the question presented on appeal was whether medical testimony that a disease possibly, as distinguished from probably, caused or contributed to death is sufficient to support a finding that it did.

So far as we have been able to discover, said the court, the question in this precise form has never been considered by any California appellate court. The rule appears to be consistently followed in other jurisdictions of this country where the question has arisen "that medical testimony as to the possibility of a causal relation between a given accident or injury and the subsequent death or impaired physical or mental condition of the person injured is not sufficient, standing alone, to establish such relation." In a prior California case it was said, "It is also true that to justify an award there must be an affirmative showing of a case within the statute and it must affirmatively appear that there exists a reasonable probability that the employee contracted the disease because of his employment." The appellate court admitted that medical testimony of possibility plus other evidence may be sufficient to support a conclusion of probability. The only other evidence in this case, however, was that of the physical symptoms of the employee before and during his last illness, and those symptoms were as characteristic of meningitis as of lead encephalitis. They therefore, concluded the court, furnish no independent evidence on which the commission could have relied, since the employee admittedly died of meningitis.

Accordingly the court held that the medical showing of a mere possibility that death resulted from lead poisoning was insufficient and the award of the Industrial Commission was annulled. *Travelers Insurance Company v. Industrial Accident Commission, 195 P. (2d) 48 (Calif., 1948).*

Workmen's Compensation Acts: Compensation Award as Bar to Malpractice Action.—This was an action for damages alleged to have been caused by the malpractice of the defendant physicians. The case was heard in the supreme court of New Jersey, Bergen County.

The plaintiff, while an employee of the Wright Aeronautical Corporation, received an injury to the index and second fingers of her right hand, arising out of and in the course of her employment. She was taken immediately to the defendants, the plant physicians, and received medical treatment from them for about two months. Some time after that she became dissatisfied with the manner in which the fractured bone in the finger was reduced by the defendants and had the job redone by a physician and surgeon of her own selection, whose bill for such services was paid by the employer as part of the compensation award. A subsequent application for a compensation award resulted in the granting of awards for both temporary and permanent disability, which awards were accepted by the plaintiff. The plaintiff then commenced this action for malpractice, contending that the plant physicians were negligent in the diagnosis and treatment of her injury. The defendants contended that the plaintiff, by accepting the compensation award, was barred from maintaining the present action.

Assuming that the defendants were negligent in the treatment of the plaintiff's injured fingers, that negligence, said the court, simply aggravated the original industrial injury. The employer was responsible in compensation for the whole injury. Since the ultimate disability, continued the court, is classable as resulting from the first injury, in that it came about through treatment of that injury and was directly connected therewith, the original industrial mishap and its assumed aggravation by the defendants should therefore be classified as one and the same compensable injury. The court then pointed out that the workmen's compensation act imposes liability for compensation on the employer regardless of fault and provides an exclusive remedy to employees for accidental injuries arising out of and in the course of employment. In accordance therewith, full compensation was paid by the employer and accepted by the plaintiff for the disability attributable to her original injury. She is entitled, concluded the court, to only one satisfaction for that injury. Here, at best, the injury was aggravated by the alleged negligence of the plant physicians. The remedy provided by the compensation act is exclusive, and any aggravation of the original injury not caused by an independent, intervening act is considered compensable. The plaintiff's right of action for negligence against the plant physicians was therefore barred by the acceptance of the compensation award, and the case was accordingly dismissed.—*Burns v. Vilardo, 60 A. (2d) 94 (N. J., 1948).*

Council on Medical Education and Hospitals

NEW HOSPITALS REGISTERED

The following hospitals were registered by the Council on Medical Education and Hospitals of the American Medical Association at its meeting in Chicago, Oct. 16-17, 1948:

Marvin Kendrick Memorial Hospital	Luverne, Ala.
Garden Grove Sanitarium	Garden Grove, Calif.
Oakdale Municipal Hospital	Oakdale, Calif.
University of Denver Hospital	Denver
Florida State Hospital No. 2	Arcadia, Fla.
H. C. White Clinic-Hospital	Fort Walton, Fla.
Suwannee County Hospital	Live Oak, Fla.
Dr. Strange's Hospital	McIntosh, Fla.
Bay Hospital	Valparaiso, Fla.
Jubal Watts Memorial Hospital	Bowdon, Ga.
Haralson County Hospital	Buchanan, Ga.
McCoy-Jackson Hospital	Folkston, Ga.
Idaho State Elks Convalescent Home for Children	Boise, Idaho
Sun Valley Hospital	Sun Valley, Idaho
Haws Memorial Hospital	Fulton, Ky.
Our Lady of the Way Hospital	Martin, Ky.
Mary Chiles Hospital	Mount Sterling, Ky.
Montelepre Hospital-Clinic	New Orleans
Physicians and Surgeons Hospital	Shreveport, La.
Hardtner Memorial Clinic-Hospital	Urania, La.
Deer River Hospital	Deer River, Minn.
Sisters of Charity Hospital	Jackson, Minn.
Louisville Hospital	Louisville, Miss.
Beacham Memorial Hospital	Magnolia, Miss.
Bales Hospital	Carrollton, Mo.
Lodge of the Turquoise Trail	Albuquerque, N. M.
Davie Hospital and Clinic	Farmington, N. M.
Reeves Clinic-Hospital	Hope Mills, N. C.
Peoples Hospital	Mansfield, Ohio
Carver Memorial Hospital	Chattanooga, Tenn.
Medical and Surgical Hospital	Brady, Texas
Camden Hospital	Camden, Texas
St. Edward Hospital	Cameron, Texas
Jones Eye, Ear, Nose and Throat Hospital	Dallas, Texas
Plains Memorial Hospital	Dimmitt, Texas
Dublin Hospital	Dublin, Texas
Memorial Hospital	Dumas, Texas
Freeport Hospital	Freeport, Texas
Hearne Clinic-Hospital	Hearne, Texas
Gonzales Warm Springs Foundation Hospital	Ottine, Texas
Ogden Hospital	Pleasanton, Texas
Fisher County Memorial Hospital	Roby, Texas
Whitney Memorial Hospital	Whitney, Texas
Winters Municipal Hospital	Winters, Texas

Miscellany

FREEDOM TO PURSUE TRUTH EXEMPLIFIED IN DISCOVERY OF THE Rh FACTOR

Condensed from a Special Lecture in Pathology delivered at the University of London by D. F Cappell, M.D., and published in the *Glasgow Medical Journal*, August 1948.

Less than fifty years ago Landsteiner discovered the three common blood groups, A, B and O, and two years later his pupils found the fourth, rarer type, now called AB. Today a bewildering array of blood groups confronts the student, the ABO system, MN and P types, the Rh groups, the four less often detected Lutheran, Levay, Kell and Lewis red cell antigens and doubtless others which await the means of accurate detection. The ABO and Rh groups are always important clinically; the others only occasionally.

There is a lesson in the way in which these discoveries were made. The clinical conditions now recognized to be associated with Rh incompatibility had been known for many years. In 1892, Ballantyne described generalized dropsy of the fetus with all the pathognomonic features including the increased size of the placenta. Then in 1909 Buchan and Comrie described the extramedullary hemopoiesis of familial icterus gravis. Ecklin in 1919 recorded the first accurate observations on congenital hemolytic anemia. In 1932, Diamond, Blackfan and Baty correlated the pathologic findings in all three fetal disorders and described the essential unity of their pathogenesis. However, it was Parsons, Hawksley and Gittens who in 1933 first recognized the essentially hemolytic nature of these disorders and pointed out that the erythroblastosis which had misled other observers was merely a compensatory mechanism. Time has shown that they were right. In 1938, Darrow suggested that the phenomena could best be explained on the basis of an antigen-antibody reaction. In 1939, Levine and Stetson detected an irregular agglutinin in the serum of a woman who had given birth to a stillborn child and suggested that she might have been immunized by an antigen from the fetus. Thus, the problems of erythroblastosis of the newborn were widely recognized, but they had not yielded the secret of etiology.

A point of fundamental importance is that the solution of the etiology of this type of clinical mystery arose entirely as an unexpected by-product from purely academic scientific work. Landsteiner's fundamental observations on the blood groups originated directly from the discovery of specific biochemical differences between species when he endeavored to determine whether within one species similar, if slighter, individual differences could also be demonstrated. He was quick to see the usefulness of his discovery and to advocate the selection of donors for transfusion on the basis of the compatibility of the blood groups of donor and recipient. The discovery that blood groups existed and that they must be taken into account in blood transfusion was therefore an unexpected windfall from fundamental biologic research. Continuing the pursuit of pure knowledge on the distribution of the M agglutinogens in human and in animal erythrocytes, Landsteiner and Weiner in 1940 announced the discovery of the Rhesus factor. Once again the clinical significance of the new knowledge was rapidly recognized and, as the basis of treatment, has been the means of saving many lives.

In these days of an impending state medical service (England—Ed.) and so-called planning, scientific workers must not be too slavishly restricted to prescribed *ad hoc* lines, but must be given freedom and support to pursue truth as an end in itself. This research on blood groups corroborates what is common knowledge among men of science everywhere, but the public does not sufficiently realize how much of our heritage of benefit discovery has been a side issue, unsuspected when the work began.

Medical Motion Pictures

FILM REVIEWS

The Preparation of Diphtheria Antitoxin and Prophylactics. 16 mm., black and white, sound, 1,300 feet (1 reel), showing time thirty-five minutes. Prepared in 1944, by H. J. Parish, M.D., and A. J. Glenny, Wellcome Physiological Research Laboratories. Produced by the G. B. Instructional, Ltd. Procurable on loan from: Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10.

This film reviews and presents in logical sequence the development of diphtheria antitoxin and toxoids. It was produced in England under war time conditions. Certain principles in immunology are stressed. The producer has attempted to incorporate all phases of the problem, and, as a result, the picture is rather long and detailed. There is no mention made of the use of penicillin in the treatment of diphtheria.

The film is suitable as a supplement to lectures offered students in bacteriology, beginning classes in immunology, public health students, nurses and technicians. It is not recommended for practitioners or interns. The photography and animation are well done.

Cesarean Section—Norton Paravesical Extraperitoneal Technic with a Case History. 16 mm., color, silent, 600 feet (1 reel), showing time fifteen minutes (sound speed). Prepared in 1948 by Milton McCall, M.D., and Arthur First, M.D., Department of Obstetrics & Gynecology, Jefferson Medical College, Philadelphia. Procurable on loan from Milton McCall, M.D., 1814 Spruce Street, Philadelphia 3.

The Norton technic for cesarean section is well depicted in this motion picture. Following the dissection of the paravesical fascia, the edge of the bladder and the exposure of the lower uterine segment are clearly demonstrated.

This is a good production, and little time is wasted with unnecessary remarks. It should prove useful for teaching obstetricians, general surgeons who do cesarean operations in neglected cases and residents and interns who plan to specialize in obstetrics and gynecology.

The titles are clear and the color photography is excellent.

The Use of Digitalis in Heart Failure. 16 mm., color, sound, 1,200 feet (1 reel), showing time thirty-five minutes. Prepared in 1947 by the Department of Pharmacology, Cornell University Medical College, New York Hospital, New York. Produced by Transfilm, Inc., New York. Procurable on loan from: Wyeth, Incorp., 1600 Arch Street, Philadelphia 3.

This film is a combination of a lecture, straight photography and animation depicting the prognosis of cardiac failure with the use of digitalis and digitoxin as observed by the Cornell group. Some cardiologists may disagree with some of the conclusions drawn; however, this group has been a major contributor in this field, which justifies their authority in the use of this agent.

The production could be made shorter by taking out certain sequences without destroying the purpose of the film; otherwise the film is well planned. It is suitable for showing to cardiologists, general practitioners, interns and medical students. Photography is excellent.

SELECTED LIST OF MOTION PICTURES

The department of rehabilitation and physical medicine of the New York University College of Medicine has prepared a list entitled "A Selected List of Motion Pictures on Rehabilitation and Physical Medicine." It contains about seventy-five motion pictures in rehabilitation and physical medicine screened and evaluated by the staff of the department of rehabilitation and physical medicine at Bellevue Hospital. The list does not include all the films available in this field, since some were considered obsolete or of minimal value and others have not as yet been reviewed. Copies of this list may be obtained by writing directly to the New York University–Bellevue Institute of Rehabilitation and Physical Medicine, 325 East Thirty-Eighth Street, New York 16.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

215:479-598 (May) 1948

Special Methods for Diagnosis of Tumors in Laboratory. N. C. Foot. —p. 479.
*Folic Acid Therapy: Results of Clinical Study. W. S. Adams and J. S. Lawrence.—p. 487.
Pharmacodynamic Properties of Penicillin Preparations with Prolonged Action. N. Ercoli, W. C. Hueper, L. Landis, Mary M. Lewis and others.—p. 498.
*Single Injection Treatment of Gonorrhea with Potassium Penicillin Suspension in Oil-Containing Epinephrine. A. Cohn and B. A. Kornblith. —p. 506.
Effectivness of Penicillin in Treatment of Nasopharyngeal Diphtheria. E. W. Bixby.—p. 509.
Clinical Evaluation in Children of Toxicity and Efficacy of Caronamide (4-Carboxyphenylmethanesulfonanilide) for Competitive Inhibition of Penicillin Excretion. M. Rapoport, F. B. Corneal, K. H. Beyer and W. F. Verwey.—p. 514.
Myelophthisic Anemia Presenting Manifestation of Prostatic Carcinoma with Skeletal Metastases: Effect of Castration and Stilbestrol. R. R. Commons and M. B. Strauss.—p. 525.
Antihistaminic, Antianaphylactic and Antiallergic Activity of N-(a-Pyridyl)-N-(a-Thenyl)-N', N'-Dimethyl-Ethylenediamine Hydrochloride. A. S. Friedlaender and S. Friedlaender.—p. 530.
Perforation of Infarcted Interventricular Septum: Report of Two Cases, One Diagnosed Antemortem. N. O. Fowler Jr. and R. B. Failey. —p. 534.
Use of Vitamin E in Heart Disease. S. Baer, W. I. Heine and D. B. Gelfond.—p. 542.
*Osteoporosis Occurring During Potassium Thiocyanate Therapy for Hypertensive Disease. J. J. Hinchey, E. A. Hines and R. K. Ghormley. —p. 548.
Blood Volume Changes and Available (Thiocyanate) Fluid Space in Soldiers with Chronic Wound Infections and Associated Nutritional Depletion. W. S. M. Ling and H. Sprinz—p. 555.
Roentgenologic Evidence of Biliary Regurgitation: Roentgenologic Contributions to Diagnosis of Hypoparathyroidism, Appendicitis, Mesenteric Thrombosis. H. M. Weber.—p. 568.
Pharmacodynamic Considerations of Atropine and Related Compounds. H. C. Stoll.—p. 577.

Folic Acid Therapy.—Adams and Lawrence report on administration of folic acid in a variety of hemopoietic disorders including addisonian pernicious anemia, tropical sprue, macrocytic anemia of unexplained origin, anemia of renal insufficiency, leukemia, idiopathic leukopenia, irradiation leukopenia associated with cancer and leukopenic states of Addison's disease, Felty's syndrome and thiouracil intoxication. Thirty-four cases in all have been studied. It was found that folic acid will correct the abnormal blood changes in cases of pernicious anemia in relapse, but the neurologic manifestations of pernicious anemia are not corrected by folic acid. The reticulocyte response in liver-treated patients with pernicious anemia differs from that obtained in folic acid-treated patients. It is probably unwise to combine folic acid and iron in the treatment of pernicious anemia. One case of sprue responded favorably to administration of folic acid. Not all macrocytic anemias respond to the administration of folic acid, but in cases in which there is a megaloblastic arrest in the bone marrow, favorable results can be anticipated. Folic acid did not affect the anemia associated with chronic nephritis, and it did not alter the leukopenia associated with either Addison's disease or Felty's syndrome (1 case each). The apparent effect of folic acid on the level of granulocytes in 1 case of agranulocytosis due to thiouracil was probably coincidence, for others have reported no effect. Folic acid had no effect on the leukopenia of idiopathic states, and no beneficial effect was noted in 2 cases of leukemia treated with folic acid. Folic acid did not correct the leukopenia induced by roentgen radiation.

Penicillin in Oil with Epinephrine for Gonorrhea.—Cohn and Kornblith investigated the effectiveness of a single injection of potassium penicillin in oil containing epinephrine in the treatment of gonorrhea. They found that a single injection of 150,000 units intramuscularly or subcutaneously, in a total volume of 0.5 cc., cured 97 of 100 patients. The 3 patients who did not respond to the initial injection were promptly cured with a second injection of an identical amount of penicillin. All of 19 patients who were treated with 200,000 units in 1 cc. intramuscularly were cured. Likewise all of 18 patients treated with 300,000 units in 1 cc. and all of 9 patients treated with 600,000 units in a total volume of 2 cc. responded to this form of therapy. No untoward local or systemic reactions were observed after the subcutaneous or intramuscular injection of the suspension of crystalline potassium penicillin in oil with epinephrine.

Osteoporosis Occurring During Potassium Thiocyanate Therapy of Hypertension.—Hinchey and his colleagues observed occasional instances of osteoporosis and arthralgia after extensive use of potassium thiocyanate in the treatment of hypertension. The records of 5,000 consecutive patients with hypertension who had been seen on two or more occasions at the Mayo Clinic in the period 1939 to 1944, inclusive, were reviewed. Potassium thiocyanate had been given to 360 patients of this group. Unexplained osteoporosis occurred in 7. Since 1944 there have been 4 additional patients with this syndrome. No history of trauma or injury at onset could be elicited from these patients. One or more extremities, usually the lower, were involved. Evidence at hand seems to suggest slight and prolonged interference with calcium metabolism as a possible mechanism for production of the syndrome. Adequate calcium intake should be assured for persons taking potassium thiocyanate. Use of this drug may be contraindicated in the presence of bone malacia, such as senile osteoporosis or osteitis deformans; likewise its use may be inadvisable in the presence of fracture, not as regards union of the fracture but because any interference with calcium metabolism in the presence of increased calcium requirement might precipitate osteoporosis.

American Journal of Medicine, New York

5:1-164 (July) 1948

*Antistreptolysin "O": Study of This Antibody in Health and in Hemolytic Streptococcus Respiratory Disease in Man. L. A. Rantz, Elizabeth Randall and Helen H. Rantz.—p. 3.
Streptococcal Fibrinolysin (Streptokinase): Study of This Substance and Its Antibody in Group A Hemolytic Streptococcus Sore Throat. L. A. Rantz and P. J. Boisvert.—p. 24.
Immediate Pressor Effect of Desoxycorticosterone Acetate in Arterial Hypertension. M. L. Goldman and H. A. Schroeder.—p. 33.
Prolongation of Coagulation of Whole Blood by Dicumarol in Man. W. C. Moloney, A. S. Murphy and W. J. Harrington.—p. 40.
Thephorin in Allergy: Study of 292 Cases. E. B. Cohen, Helen P. Davis and W. A. Mowry.—p. 44.
Agranulocytosis During Propylthiouracil Therapy. E. C. Bartels.—p. 48.
Acute Porphyria: Two Cases with Autopsy Reports. Laura Hare and R. Wilmore.—p. 53.
Spontaneous Mediastinal Emphysema and Pneumothorax. A. J. Draper. —p. 59.
Pyoderma Gangrenosum in Chronic Non-Specific Ulcerative Colitis: Report of 3 Cases. W. E. Ricketts, J. B. Kirsner and S. Rothman. —p. 69.
Unusual Strain of Pseudomonas Aeruginosa Recovered from Urinary Bladder: Effects of Streptomycin. J. A. Lazarus and L. H. Schwarz. —p. 76.
What Value Enteric Coating. J. B. Wolffe.—p. 87.

Antistreptolysin "O" in Health and Respiratory Disease.—According to Rantz and his associates antistreptolysin "O" is an immune substance which neutralizes streptolysin "O" in vitro. It is contained in the gamma globulin fraction of human serum. Its concentration in the serum of healthy persons and its formation after infection in young adults by group A hemolytic streptococci has been studied. The amount of this substance in serums obtained from healthy persons varies with the geographic area of residence of the subjects and their age. Antibody levels are low through the second year of life, rise rapidly through the first decade and then decline. In studies on the mechanics of antistreptolysin response in large numbers of group A hemolytic streptococcus sore throat, it was noted that an increase in this antibody occurred regularly after infection by these organisms. The amplitude of the response varied from patient to patient, but the peak level was reached by the fourth week after the onset of acute illness in nearly all cases. No relationship between the initial antistreptolysin titer and the nature of the acute suppurative phase of hemolytic strepto-

coccus sore throat was demonstrated, but a definite correlation between the magnitude of antistreptolysin response, severity of the initial illness and the later development of nonsuppurative complications was demonstrated. Immunologic differences were established between uncomplicated group A hemolytic streptococcus infection of the respiratory tract and that which initiates a nonsuppurative disorder. An exaggerated mean antistreptolysin response occurred in all clinical categories of the latter group. In addition, the antistreptolysin titer at the onset of the initial streptococcic illness was somewhat higher, and antibacterial precipitating antibodies were present with unusual frequency in patients who later contracted arthritis. The abnormal production of these antibodies may mirror an exaggerated immunologic hyperreactivity of human beings in whom these disease states develop.

American Journal of Orthopsychiatry, New York

18:381-570 (July) 1948. **Partial Index**

Trends in Orthopsychiatric Therapy. L. G. Lowrey and others.—p. 381.
Conscience in the Psychopath: Another Version. B. Karpman.—p. 455.
Emotional Problems in "Planned For" Children. Sophie Schroeder Sloman. —p. 523.
Child Guidance Services in Semi-Rural and Neglected Areas: Public Health Project in Wisconsin. Eugenia S. Cameron.—p. 536.
New Partnerships for Psychiatry. C. Binger.—p. 543.
Anxiety Neurosis. S. Sheplow.—p. 548.

American Journal of Physiology, Baltimore

153:1-196 (April) 1948. **Partial Index**

Proof of Hormonal Mechanism for Gastric Secretion—Humoral Transmission of Distention Stimulus. M. I. Grossman, C. R. Robertson and A. C. Ivy.—p. 1.
Adrenal Cortex and Altitude Tolerance. F. J. Kottke, C. B. Taylor, W. G. Kubicek and others.—p. 16.
*B Vitamin Requirements with Advancing Age. C. A. Mills.—p. 31.
Kidney and Nitrogen Metabolism. E. Mylon, E. R. Smith and P. Goldstein.—p. 55.
Fluid Shifts During Exposure to Accelerations: Rapid Local Changes Under Negative G. F. Stauffer and C. Hyman.—p. 64.
Sequential Changes in Oxygen Consumption During Oligemic and Normovolemic Shock and Their Meaning. R. S. Post, P. H. Visscher and C. J. Wiggers.—p. 71.
Effect of Pentothal Sodium on Blood Gas Transport. K. E. Penrod and A. H. Hegnauer.—p. 81.
Metabolic Changes of Resting Potential in Relation to Action of Carbon Dioxide. A. M. Shanes.—p. 93.
Effect of Repeated Denervation on Neuromuscular Function. J. A. Morgan, J. D. Thomson and H. M. Hines.—p. 109.
Role of Acetylcholine in Activity of Sensori-Motor and Suppressor Areas of Cortex. S. Beckett and E. Gellhorn.—p. 113.
Effect of Age on Lethality of Di-Isopropyl Fluorophosphate. A. M. Freedman and H. E. Himwich.—p. 121.
Antithrombic and Antiproteolytic Activity of Alpha Tocopheryl Phosphate. K. L. Zierler, D. Grob and J. L. Lilienthal Jr.—p. 127.
Influence of Dosage of Xanthopterin on Response in Hemapoiesis. E. R. Norris and J. J. Majnarich.—p. 133.
Residual Lung Volume Determinations by Methods of Helium Substitution and Volume Expansion. T. L. Willmon and A. R. Behnke. —p. 138.
Effect of Bile Diversion on Fecal Fat and Nitrogen Excretion. J. R. Heersma and J. H. Annegers.—p. 143.
Changes in Blood Leukocyte Level of Adrenalectomized and Normal Rats Following Administration of Typhoid Vaccine. Lena A. Lewis and I. H. Page.—p. 148.
Changes in Arterial Inflow in Dog's Leg Following Venous Occlusion: Evaluation of Results Obtained with Different Types of Flow Recorders. D. E. Gregg, W. H. Pritchard and R. E. Shipley.—p. 153.
Effects of Percutaneous Stimulation on Circulation in Normal and in Paralyzed Lower Extremities. K. G. Wakim, Jean C. Terrier, E. C. Elkins and F. H. Krusen.—p. 183.

B Vitamin Requirements with Advancing Age.—Mills observed greatly increased thiamine requirement in milligrams per kilogram of diet with advancing age in rats. Rafsky and Newman have described an apparent thiamine deficiency in aged persons on diets which are qualitatively quite adequate for young adults. Mills says that at his laboratory a group of rats has been followed from weaning time to old age, being tested periodically for their requirement of one B vitamin after another needed for optimal growth. The increase in thiamine requirement with advancing age in rats was further verified. None of the other B vitamins studied (choline, pyridoxine, riboflavin and pantothenic acid) gave evidence of similar increase in requirement with advancing age. The author concludes that these observations, in conjunction with studies on aged persons, provide reason to recommend thiamine supplementation for elderly persons.

American Practitioner, Philadelphia

2:703-770 (July) 1948

Physiologic Therapy of Intractable Bronchial Asthma and Status Asthmaticus, Part II. A. L. Barach.—p. 703.
Malignant Hypertension. R. Birchall.—p. 713.
Cervical Disk Syndrome. A. Fields.—p. 724.
*Coronary Deaths in "Healthy" Young Soldiers: Clinicopathologic Study. N. E. Reich.—p. 731.
Cystinuria: Case Report. S. D. Ezell.—p. 748.
Untoward Reactions of Therapy with Gold. R. R. Kierland.—p. 750.
Hypodermic Needles Stored in Eye Droppers. C. B. Strauch.—p. 752.
Dermatitis Following Ingestion of Pyribenzamine. H. Rattner and J. Graffin.—p. 754.

Coronary Death in Young Soldiers.—Reich reports the occurrence of coronary death in 11 male soldiers between the ages of 22 and 38. The length of military service ranged from one month to forty-three months. Atherosclerosis was responsible for the fatal outcome in 10 cases, 2 of which revealed no thrombosis. One patient had coronary embolism with arteritis and septic thromboses of the smaller coronary branches. Overweight was a predisposing factor in 7 patients. Contrary to the classical description of onset at night, all the patients were attacked during the waking hours. In 6 the onset was unassociated with strenuous activity. Unusual prodromes due to the reflex symptoms referable to other systems, especially the gastrointestinal tract, accounted for the main difficulty in correct diagnosis. Although these patients had been examined on numerous occasions and were considered in good health, varying degrees of clinically undiagnosed cardiac enlargement were present in 6 of them at necropsy. When extra physical demands are made in war or heavy industry, it may be advisable to add electrocardiographic studies with oxygen deprivation tests to routine laboratory examinations for the earlier diagnosis of coronary insufficiency.

Annals of Allergy, Minneapolis

6:219-352 (May-June) 1948

Psychodynamics and Allergic Patient. H. A. Abramson.—p. 219.
Skin Tests with Endocrine Substances: Method of Zondek and Bromberg. R. L. Laer, V. H. Witten and J. R. Allen.—p. 239.
*Fever Due to Food Allergy. A. H. Rowe.—p. 252.
Mold Distribution in Air and Dust in Kentucky. Anna Newton, M. Scherago and R. H. Weaver.—p. 260.
Bacteriologic Studies of Multiple Sclerosis. E. C. Rosenow.—p. 271.
RH Factor in Immunologic Reactions. A. S. Wiener.—p. 293.
Clinical Evaluation of Neohetramine, a New Antihistamine. G. L. Waldbott and R. Borden.—p. 305.
*Dermatophytosis and Fungus Sensitivity. S. H. Jaros and M. H. Kirsner. —p. 307.
Paroxysmal Dyspnea: Case Report. H. S. Bernton.—p. 317.

Fever Due to Food Allergy.—Rowe directs attention to food allergy as one cause of unexplained fever. Failure to recognize food allergy as one cause of fever accounts for some unjustifiable diagnoses of idiopathic or psychogenic fever, subclinical tuberculosis, brucellosis or other questionable infections. It has led to unnecessary operations on tonsils, appendixes, gallbladders and pelvic organs. Needless surgical operations have been performed on nasal sinuses because of the association of fever with nasal congestion, blocking or postnasal mucus, and especially with swollen membranes or opacities in the antrums or other sinuses which were not due to infection but to allergy. The author reports the case of a girl, aged 18, who had prolonged allergic fever that was preceded by lifelong anorexia, aversion for milk, and recent colonic symptoms. Because of this fever, the patient was hospitalized for four and one-half months. During this time many laboratory and clinical investigations were conducted, and at one time a presumptive diagnosis of psychogenic fever was made. The relief from her fever, from the colonic and anal symptoms and from the fatigue and the other toxic symptoms by use of the elimination diet, and their subsequent reproduction by the ingestion of milk, prove that food allergy was responsible. Her initial colonic symptoms suggested the onset of a possible chronic ulcerative colitis, which, in the writer's opinion, is frequently due to food allergy. If the allergy had not been recognized, more definite tissue changes due to chronic ulcerative colitis might have developed. The most likely explanation of allergic fever is a disturbance in the temperature-regulating center of the brain by a localized or generalized allergic reaction.

Dermatophytosis and Fungus Sensitivity.—Jaros and Kirsner present immunologic evidence bearing on the close relationship between the sensitivity to fungus extracts in patients having a fungous infection. They treated patients with epidermophytoses and epidermophytid by means of a fungus extract containing Trichophyton gypseum, Trichophyton interdigitale, Epidermophyton inguinale and Monilia albicans in a dilution of 1:5,000. Since all these fungi do not interreact, a composite mixture had to be made in order to cover the most common causative fungus factors. Thirty patients are presented who were followed for a period of about a year. All had received previous local therapy. Etiologic organisms were cultured and identified. Each patient received a dose of 0.1 cc. of the extract intradermally twice a week. This schedule was attended by good results. In extremely sensitive patients, the extract was further diluted or a smaller dose given. In those who had improved greatly the interval between injections was increased to one week. In 2 patients an attempt was made to increase the dosage in order to shorten the course of therapy. It was found that if more than 0.2 cc. was injected intradermally, local necrosis would result, with the skin over the wheal sloughing off. No serious reactions were seen after injection, although there were occasional and temporary flaring up of the lesion, local reaction at the site of injection associated with a mild lymphadenitis and pruritus. More than 80 per cent of the patients were greatly improved or cured after this desensitization.

Annals of Internal Medicine, Lancaster, Pa.

29:1-220 (July) 1948

Modification of Fat Absorption in Digestive Tract by Use of Emulsifying Agent. C. M. Jones, P. J. Culver, Gladys D. Drummey and Anna E. Ryan.—p. 1.
Heart Failure: Relation of Symptoms and Signs to Its Severity and Duration. W. Dock.—p. 11.
Shoulder-Hand Syndrome in Reflex Dystrophy of Upper Extremity. O. Steinbrocker, N. Spitzer and H. H. Friedman.—p. 22.
Action of Neostigmine in Supraventricular Tachycardia. S. Waldman and L. Pelner.—p. 53.
*Observations on Use of Respirator in Refractory Status Asthmaticus. M. F. Reiser and E. B. Ferris Jr.—p. 64.
Treatment of Cardiovascular Syphilis. H. Eisenberg.—p. 71.
Management of Diabetes Mellitus: Analysis of Present-Day Methods of Treatment. H. O. Mosenthal.—p. 79.
*Prognostic Significance of "Guillain-Barré Syndrome." M. Hand and M. Rudoy.—p. 91.
*Meningitis Due to Pseudomonas Pyocyanea: Report of Three Cases Treated Successfully with Streptomycin and Sulfadiazine. L. Weinstein and T. S. Perrin.—p. 103.
Challenge of Preventive Medicine. J. S. Simmons.—p. 118.
Preliminary Report on Beneficial Effect of Chloromycetin in Treatment of Typhoid Fever. T. E. Woodward, J. E. Smadel, H. L. Ley Jr., R. Green and others.—p. 131.

Use of Respirator in Refractory Status Asthmaticus.—Reiser and Ferris used anesthesia and the Drinker respirator for artificial respiration in 3 patients with acute intractable asthma. Since expiration is primarily limited in asthma, it would appear that the best procedure for the maintenance of adequate ventilation would be to support this phase. This can be effectively accomplished by the use of the Drinker respirator which applies positive pressure to the chest wall and abdomen. Since the respirator also aids inspiration, inspiratory dyspnea is at the same time decreased. In each of the 3 cases, prompt and satisfactory relief of anoxemia was accomplished and maintained until bronchiolar spasm had undergone remission. One patient was treated early in the course of his attack and recovered uneventfully. The 2 others died, but the unfavorable outcome can be explained on the basis of complicating factors and need not to be regarded as indicating failure of treatment with the respirator. While no definite conclusion can be drawn from limited experience, it is felt that the rationale is sufficiently clear, and the results, so far as relief of anoxemia is concerned, are gratifying enough to warrant the use of the respirator in refractory status asthmaticus. It is of utmost importance that the therapy be instituted early in the course before irreversible changes have appeared, or other grave complications have had time to gain foothold. This maneuver is not suggested as a substitute for other well established methods of treatment, but rather as an adjunct in refractory cases.

"Guillain-Barré Syndrome."—Hand and Rudoy report 11 cases of polyneuritis observed in American soldiers abroad between the ages of 20 and 41, 10 of whom had a definite history of pharyngitis, which preceded the onset of neurologic disturbance by three to six weeks. All were characterized by diminution of motor power, reflexes and sensibility in the extremities. Accommodation and swallowing difficulties were common at the onset, and some urinary disturbances were noted. Elevation of the total protein content of the spinal fluid without increase of cells was present in every case. In 6 of the 11 patients an exacerbation of symptoms occurred after partial recovery. Two cases of polyneuritis in American civilians in New York, occurring one month after a severe sore throat in one case and in the other two months after pyodermia, had a similar course to that of the 11 soldiers. Five additional cases of polyneuritis in German prisoners of war are reported whose throat smears revealed the presence of diphtheria bacillus. In these patients the total protein of the spinal fluid was normal or only slightly elevated. Similarly in 4 additional German prisoners with polyneuritis associated with extraordinary ingestion of sulfonamide drugs over a long period there was no elevation of the total protein in the spinal fluid. Fever was not present in any of the cases in association with the neurologic disability, but was present in rare instances at the time of throat infection weeks before. Spontaneous pains or burning sensations occurred, but were not common in this series. Treatment consisted of bed rest, physical therapy from the onset of motor weakness, thiamine chloride 300 mg. daily, with a diet high in vitamins. Activity was permitted to the extent of the patient's capability. All the patients recovered and none was left with disabling residua. Minimal febrile reaction, symmetry of limb involvement and the occurrence of subjective and objective sensory changes differentiate the syndrome clinically from anterior poliomyelitis. The spinal fluid findings offer definite diagnostic evidence. Postdiphtheritic neuritis closely resembles the Guillain-Barré syndrome, as has been shown in the 5 cases of polyneuritis in the German prisoners with diphtheria bacilli. Differentiation depends on demonstration of diphtheria bacilli and on the relatively slight elevation of total protein in the spinal fluid. Etiologic relationship with throat infections such as tonsillitis, exudative pharyngitis of streptococcic or diphtheritic origin and pyemia is apparent. Sulfonamide drugs used in treatment of these primary infectious conditions may on occasion constitute the etiologic agents in the neurologic syndrome.

Meningitis Due to Pseudomonas Pyocyanea.—Weinstein and Perrin successfully treated 2 women aged 33 and 58 and a boy aged 16, who had primary meningitis due to Pseudomonas aeruginosa, with intrathecal and intramuscular streptomycin combined with sulfadiazine or sulfamerazine. In all the patients infection of the meninges occurred during the course of spinal anesthesia. The source of the organism could not be determined. The strains of Ps. aeruginosa responsible for the infection were sensitive to between 7.8 and 30 units of streptomycin per cubic centimeter and did not become resistant to the drug during treatment. Penicillin intrathecally was given a brief trial but was singularly ineffective. The sulfonamide drugs, used alone, also failed to control the meningeal infection, although temporary moderate improvement was produced by large doses. Streptomycin is indispensable for successful treatment of primary meningitis due to Ps. aeruginosa. Combined with sulfadiazine or sulfamerazine, it appears to be the treatment of choice. The total dose of streptomycin administered intrathecally varied from 1.8 Gm. to 8.1 Gm. and intramuscularly from 36.5 to 227 Gm. Two patients had from one to four relapses of the meningeal infection when treatment was stopped. These recurrences were accompanied by the presence of a variable number of red blood cells and occasionally by xanthochromia in the spinal fluid. Deafness occurred as a complication in all the patients, and 1 of them showed severe labyrinthine disturbance with complete loss of vestibular function. There was improvement in hearing in all the patients after discontinuation of the antibiotic therapy.

Archives of Neurology and Psychiatry, Chicago

59:273-444 (March) 1948

Organic Mental Syndrome with Phenomena of Extinction and Allesthesia. M. B. Bender, S. B. Wortis and J. Cramer.—p. 273.
Pallhypesthesia: Depression of Appreciation of Vibration in Trauma and in Disease; Preliminary Report. S. Goldblatt.—p. 292.
Psychosis Following Lobotomy in Case of Sexual Psychopathy: Report of Case. J. W. Friedlander and R. S. Banay.—p. 302.
Tensile Strength of Human Nerves: Experimental Physical and Histologic Study. C. T. Liu, C. E. Benda and F. H. Lewey.—p. 322.
Causes of Failure in Treatment with Electric Shock: Analysis of Thirty-Eight Cases. N. K. Rickles and C. G. Polan.—p. 337.
*Penicillin in Treatment of Neurosyphilis: IV. Tabes Dorsalis. L. P. Chesney and F. W. Reynolds.—p. 347.
Subdural Hematoma: Experimental Study. R. Cohn.—p. 360.
Distribution of Lesion of Brain Stem in Poliomyelitis. M. Barnhart, R. Rhines, J. C. McCarter and H. W. Magoun.—p. 368.
Peripheral Neuritis Complicating Multiple Myeloma. N. B. Kurnick and S. B. Yohalem.—p. 378.
Involutional Psychosis: Course when Untreated and when Treated with Electric Shock. P. E. Huston and Lillian M. Locher.—p. 385.
Electroencephalogram in Cerebrovascular Disease. H. Strauss and L. Greenstein.—p. 395.

Penicillin in Tabes Dorsalis.—Chesney and Reynolds treated 54 patients having tabes dorsalis with penicillin. Thirty-three of these received penicillin alone; 21, penicillin concurrently with therapeutic malaria. A comparison of the results with penicillin alone and those with malaria and penicillin indicates clearcut superiority for the combined therapy. Treatment with penicillin alone appears superior to therapy of the era before penicillin only in respect to its convenience and relative lack of toxicity. Concurrent administration of penicillin and therapeutic malaria is the most effective form of therapy for tabes dorsalis presently available.

Archives of Surgery, Chicago

56:259-444 (March) 1948

Fractures of Ankle: Analytic Historic Survey as Basis of New Experimental, Roentgenologic and Clinical Investigations. N. Lauge.—p. 259.
*Synthetic Resin—New Antacid for Treatment of Peptic Ulcer. M. Kraemer and L. H. Siegel.—p. 318.
Pseudotumor of Bone in Hereditary Pseudohemophilia. H. S. J. Walker and N. A. Womack.—p. 329.
*Is Chronic Cystic Mastitis a Precancerous Lesion? Ten Year Follow-Up Study of 26 Cases. H. L. Reed.—p. 338.
Nocturnal Gastric Secretion: Studies on Normal Subjects and on Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma. E. Levin, J. B. Kirsner, W. L. Palmer and Carrie Butler.—p. 345.
Surgical Approach to Hypertensive Vascular Disease: Technic of Operation, Discussion of Complications and Method of Prevention. H. G. Pretty.—p. 357.
*Treatment of Peptic Ulcer with Enterogastrone. H. M. Pollard, M. Block, W. H. Bachrach and Joyce Mason.—p. 372.
Peritoneal Reaction to Oxidized Cellulose. E. T. Dmytryk.—p. 386.
Application of Delayed Suture in Management of Wounds. K. F. Lowry.—p. 393.
Review of Urologic Surgery. A. J. Scholl, F. Hinman, A. B. Hepler and others.—p. 401.

Synthetic Resin for Peptic Ulcer.—Kraemer and Siegel used "amberlite IR IV" in 60 cases of peptic ulcer and find that it is just as satisfactory as the usually employed metallic salt antacids and has few of their disadvantages. It causes neither constipation nor diarrhea. Patients have taken from 2 to 9 Gm. of the drug daily for six to eight months with no evidence of toxicity. Damage to the gastric mucosa was not noted in 3 patients in whom the stomach was resected and in 3 on whom gastroscopy was performed. It approaches the ideal antacid in that it is not absorbed from the digestive tract, has no effect on the acid-base balance and does not alkalize the urine. It neutralizes acid rapidly and promptly relieves pain. It is effective in small dosage and is inexpensive and tasteless.

Is Chronic Cystic Mastitis A Precancerous Lesion?—Reed says that since 1925 many cases of chronic cystic mastitis have been studied at Wichita hospitals. Three types of chronic cystic mastitis can be distinguished histologically: (1) simple chronic cystic mastitis, (2) chronic cystic mastitis with papillary proliferation and (3) chronic cystic mastitis with atypia. Twenty-six patients with chronic cystic mastitis who were operated on prior to 1931 were selected for follow-up study. Twenty patients had simple chronic cystic mastitis, 2 had papillary proliferation and 4 had atypia. Local excision of the involved area was performed on 23 patients, while 3 were subjected to simple mastectomy. The patients were followed for ten to seventeen years after operation, and were recently examined. One patient died of cancer of the cervix ten years after, and another of pneumonia eleven years after the operation on the breast. In neither had there been a recurrence of chronic cystic mastitis or development of cancer in the breast prior to death. One patient had two local recurrences; the lesion was excised and showed the typical picture of simple chronic cystic mastitis. During the twelve years which have followed her last operation no tumor had reappeared. The remaining 23 patients of the series are completely cured after the local excision. Carcinoma of the breast did not develop in a single instance.

Treatment of Peptic Ulcer with Enterogastrone.—Pollard and his associates treated 28 patients having peptic ulcer with enterogastrone. Twelve patients were given enterogastrone orally in doses of 8 to 16 Gm. daily for periods up to eleven months. Recurrence of typical symptoms of ulcer occurred in 2 of these patients while they were under treatment. Sixteen patients with peptic ulcer were given intramuscular injections of 200 mg. of enterogastrone daily for periods up to nine months. Three of the patients had either recurrence or persistence of symptoms while under treatment. Roentgenograms of the upper part of the gastrointestinal tract were available for 17 of the 28 patients from the start of therapy. The roentgenologic appearance of the lesion after therapy was improved in 6 patients, remained unchanged in 8 and was definitely worse in 3 patients. Single intramuscular injections of 200 and 900 mg. of enterogastrone in persons with peptic ulcer produced no changes in the volume of fasting gastric secretion, output of hydrochloride acid, pepsin concentration or gastric motility. Daily administration of enterogastrone orally or parenterally for periods up to eleven months to persons with peptic ulcer caused no significant alterations in the volume of fasting gastric secretion, volume of hydrochloric acid, pepsin concentration or type of response to a caffeine test meal. This was true whether there was evidence that the ulcer improved, remained stationary or became worse.

California Medicine, San Francisco

68:407-520 (June) 1948. **Partial Index**

Syphilis in Pregnancy. C. W. Barnett.—p. 432.
Incidence of Unsuspected Urinary Tract Infection in Selected Group of Ambulatory Women. R. H. Barr and L. A. Rantz.—p. 437.
Treatment of Urinary Tract Infections. S. Olsen.—p. 440.
Medical Treatment of Urinary Tract Infection. C. A. Noble Jr.—p. 443.
Torsion of Testicle. L. Kindall and T. T. Nickels.—p. 446.

Cancer, New York

1:1-176 (May) 1948

*Sarcoma Arising in Irradiated Bone: Report of 11 Cases. W. G. Cahan, Helen Q. Woodard, N. L. Higinbotham, and others.—p. 3.
Fibrosarcoma: Malignant Tumor of Fibroblasts. A. P. Stout.—p. 30.
Lymphangiosarcoma in Postmastectomy Lymphedema: Report of 6 Cases in Elephantiasis Chirurgica. F. W. Stewart and N. Treves.—p. 64.
Evolution of Cancer of Uterine Fundus in Rabbit. H. S. N. Greene and B. L. Newton.—p. 82.
Electrophoretic Studies on Plasma Proteins of Patients with Neoplastic Disease. Mary L. Petermann and Katherine R. Hogness.—p. 100.
Conversion of Cancer-Resistant to Cancer-Susceptible Strain of Mice by Chemical Means. L. C. Strong.—p. 120.

Sarcoma in Irradiated Bone.—Cahan and his associates point out that whereas twenty years ago radium and roentgen rays were used widely on benign and malignant tumors, either before or after operation, or both, or as the sole method of treatment, with the passage of time and the accumulation of experience the concept of the place held by irradiation in the treatment of neoplasms of bone has changed. The authors have inclined toward the belief that roentgen or radium treatment is inadvisable for benign tumors of bone. Their reasons were that surgical treatment yields more satisfactory results, that they avoid the risk of irradiating a malignant tumor under the mistaken impression that it is benign, that many of these benign lesions are either radioresistant or only slightly radioresponsive, that in children, prior to epiphysial closure, irradiation of lesions in the vicinity of growth centers may cause serious disturbances in bone growth and that an extremely serious sequel of radiation therapy is courted: there is the possibility that, after an interval of years, bone sarcoma may develop at the site of the previous irradiation. The authors summarize the

literature dealing with both experimental and clinical production of bone sarcoma by irradiation and describe 11 cases in which bone sarcoma developed at a period considerably subsequent to irradiation of benign bone tumors or of normal bone.

Cancer Research, Baltimore

7:669-740 (Nov.) 1947

Propagation of Filtrable Agents Producing Lymphoid Tumors and Osteopetrosis by Serial Passage in Chickens. B. R. Burmester and G. E. Cottral.—p. 669.
Mast Cell Reaction of Mouse Skin to Some Organic Chemicals. L. G. Larsson and B. Sylvén.—p. 676.
Mast Cells in Experimental Rat Sarcomas. H. Holmgren and G. Wohlfart.—p. 686.
Pigmented Precancerous and Cancerous Changes in Skin. V. R. Khanolkar.—p. 692.

Florida Medical Association Journal, Jacksonville

35:1-64 (July) 1948

Fenestration Operation for Otosclerosis: Analysis of One Hundred Cases. J. B. Farrior.—p. 17.
Cancer Control in Florida. W. T. Sowder.—p. 23.
Specific Treatment of Pollinosis. G. E. Henson.—p. 28.

Gastroenterology, Baltimore

10:923-1056 (June) 1948

Study of Gastric Mucosa in Various Diseases Affecting Upper Part of Gastro-Intestinal Tract. W. C. Meyers.—p. 923.
Variability and Periodicity of Nocturnal Gastric Secretion in Normal Individuals. E. Levin, J. B. Kirsner, W. L. Palmer and Carrie Butler.—p. 939.
*Comparison of Nocturnal Gastric Secretion in Patients with Duodenal Ulcer and in Normal Individuals. E. Levin, J. B. Kirsner, W. L. Palmer and Carrie Butler.—p. 952.
Burning Sensation of Tongue (Glossodynia): Analysis of Cases That are not Due to Vitamin B Deficiency. S. Waldman and L. Pelner.—p. 965.
Partial Gastrectomy: Clinical, Gastroscopic and Radiologic Considerations. M. Paulson and E. S. Glasden.—p. 970.
Gastroscopy Under Pentothal-Curare Anesthesia. S. J. Stempien and W. W. Greene.—p. 978.
Evaluation of Reliability of Certain Blood Vitamin Assays in Determining Dietary Adequacy. G. H. Laing, F. W. Jones, Dolores Anderson and J. M. Beazell.—p. 982.
Influence of Anti-Oxidative and Dispersing Agents of Vitamin A Absorption: Therapeutic Implications in Endogenous Hypovitaminemia. A. H. Popper and Hattie A. Dyniewicz.—p. 987.
Study of Vitamin A and Carotene Tolerance Tests in the Aged. H. A. Rafsky and B. Newman.—p. 1001.
Effect of Tetraethylammonium Chloride on Gastric Motility in Man. D. C. Dodds, C. L. Ould and M. E. Dailey.—p. 1007.
Recurrence of Regional Terminal Ileitis Associated with Pregnancy: Case Report. E. C. Raffensperger.—p. 1010.
Ulcerating Carcinoma of Sigmoid: Report of Case with Unusual Roentgen Picture. M. Feldman, M. E. Gann and T. Weinberg.—p. 1018.

Nocturnal Gastric Secretion.—In a previous publication Levin and his collaborators reported the results of studies on the nocturnal gastric secretion in normal persons. They now compare the data obtained in patients with active duodenal ulcer with the findings in normal subjects. They found that the volume, concentration and output of acid in the fasting nocturnal gastric secretion are usually higher in patients with duodenal ulcer than in normal persons. The volume of secretion and output of acid are usually higher during the first half of the night than during the last half. Individual variations exist. Patients with duodenal ulcer with a high volume and secretion of acid on one night in the vast majority of instances manifest a high volume and acidity on successive nights. The rate of gastric secretion is not constant, varying spontaneously from hour to hour in the same person. These variations must be taken into account in the evaluation of preparations and procedures designed to reduce gastric secretion.

Geriatrics, Minneapolis

3:197-266 (July-Aug.) 1948

Old Age: Last Stand of Tubercle Bacillus. J. A. Myers.—p. 197.
Coronary Artery Disease in Older Patients. G. F. Greco.—p. 211.
Rheumatism in the Aged. W. K. Ishmael.—p. 217.
Pentothal Sodium in the Aged with Respect to Eye Surgery. W. E. Froschauer and C. E. Schrimpf.—p. 231.
Old Age Security in Other Societies. L. W. Simmons.—p. 237.
Social and Preventive Geriatrics: Survey of Medico-Social Problems Connected with Health and Illness in Later Life. J. W. Affleck.—p. 245.

Indiana State Medical Assn. Journal, Indianapolis

7:677-780 (July) 1948

Recent Developments in Treatment of Brucellosis. D. L. Urschel.—p. 695.
Vagus Nerve Resection (Vagotomy) in Treatment of Acute Perforated Duodenal Ulcer: Report of Case. D. C. Straus.—p. 700.
Anesthesia for Patients with Disease of Cardiovascular System. W. B. Adams.—p. 703.
Ambulatory Proctology. E. L. Fitzsimmons.—p. 707.
Medical Rehabilitation Service in Veterans Administration. D. A. Covalt.—p. 716.

Journal of Aviation Medicine, St. Paul

19:137-220 (June) 1948

Etiology of Pulmonary Hemorrhage in Cats Exposed to Abrupt Deceleration. R. K. McDonald, V. C. Kelley and R. Kaye.—p. 138.
Effects of Angular Acceleration and Centrifugal Force on Nonvisual Space Orientation During Flight. K. MacCorquodale.—p. 146.
Aviator's Vertigo. W. E. Vinacke.—p. 158.
Quantitative Histochemical Changes in Adrenal Following Exposure to Anoxia. J. Nichols.—p. 171.
Certain Pharmacologic Properties of Alcohol, Nicotine and Caffeine. O. Horwitz.—p. 179.
Relationship Between Certain Aspects of Physical Fitness and Success in Pilot Training. B. E. Phillips.—p. 186.
*Studies on Removal of Gas from Colon by Oxygen Inhalation. R. S. Pogrund and F. R. Steggerda.—p. 204.
Cumulative Record of Naval Aviator Proficiency. H. E. Page.—p. 211.

Removal of Gas from the Colon by Oxygen Inhalation.—Pogrund and Steggerda point out that high blood tension of nitrogen retards the absorption of this gas from the colon, thus evolving a problem of interest to aviation physiologists; namely, the expansion of this unabsorbable gas in the intestinal tract resulting during high altitude flying. The authors studied the effect of lowering the nitrogen tension in the blood on the absorption of nitrogen from the colon by introducing 500 cc. of nitrogen into the colons of normal healthy male adult subjects. With the subjects resting, the percentage volumes of gas recovered at the end of two hours were noted, while the subjects breathed either room air (to serve as controls) or pure oxygen (to comprise the experimental study). On the basis of their observations the authors conclude that the beneficial effect of oxygen inhalation on abdominal distension is explained by the removal of nitrogen from the blood under these conditions, thereby producing a partial pressure gradient favorable for the absorption of nitrogen from the gastrointestinal tract.

Journal of Bacteriology, Baltimore

56:1-142 (July) 1948

Biochemical Mutants of Bacterial Viruses. M. Delbrück.—p. 1.
Nutrition of Brucellae: Growth in Simple Chemically Defined Media. P. Gerhardt and J. B. Wilson.—p. 17.
Studies on Anaerobic Micrococci. E. L. Foubert Jr. and H. C. Douglas.—p. 25.
Effect of Human Serum on Dilution Bioassay of Penicillins G, X and K. H. Eagle and H. A. Tucker.—p. 59.
*Origin of Bacterial Resistance to Antibiotics. M. Demerec.—p. 63.
Action of Penicillin on Staphylococcus: Further Observation on Effect of Short Exposure. R. F. Parker and Sarah Luse.—p. 75.
Pancreatic Digest Chocolate Blood Agar for Isolation of Gonococcus. Marie L. Koch.—p. 83.
Growth of Coli-Aerogenes Group in Presence of Isocitrate. S. A. Koser and G. J. Kasai.—p. 89.
Factors Influencing Production of Tetanus Toxin: Gaseous Products of Growth. J. H. Mueller, Pauline A. Miller and E. M. Lerner.—p. 97.
Cytochemical Mechanisms of Penicillin Action: VII. Effects on Activity of Alkaline Phosphatase. Jean Dufrenoy and R. Pratt.—p. 99.
Influence of Certain Substances on Activity of Streptomycin: III. Differential Effects of Various Electrolytes on Action of Streptomycin. R. Donovick, A. P. Bayan, P. Canales and F. Pansy.—p. 125.
Inhibiting Effect of Normal Serum and Its Gamma Globulin Fraction on Variation of Staphylococcus Aureus. B. F. Hoerlein.—p. 139.

Origin of Bacterial Resistance to Antibiotics.—Demerec offers evidence that bacterial resistance to penicillin and streptomycin is not induced by these compounds but originates spontaneously through genetic changes comparable to gene mutations. He describes resistance patterns observed in experiments with penicillin and streptomycin and outlines a possible mechanism responsible for resistance and for the differences between the resistance patterns observed with penicillin and those observed with streptomycin. The experiments were done in vitro. Penicillin was tested with Staphylococcus aureus, strain NRRL 313, and streptomycin was tested with the same strain of Staph. aureus and with Escherichia coli, strain B. From the knowledge

gained the author concludes that in treatment with penicillin the development of highly resistant strains can be avoided by application of penicillin in doses sufficiently large to prevent survival of first step resistant mutants. In treatment with streptomycin, however, the development of highly resistant strains cannot be prevented; effective treatment does not eliminate all bacteria, but it probably reduces their number to a level at which the organism is able to eliminate them.

Journal of Clin. Endocrinology, Springfield, Ill.

8:423-498 (June) 1948

Spontaneous and Experimentally Induced Uptake of Radioactive Iodine in Metastases from Thyroid Carcinoma: Preliminary Report. S. M. Seidlin, E. Oshry and A. A. Yalow.—p. 423.

Ageing in Apparently Normal Men: I. Urinary Titers of Ketosteroids and of Alpha-Hydroxy and Beta-Hydroxy Ketosteroids. H. B. Hamilton and J. B. Hamilton.—p. 433.

Experimental Alteration of Human Ovarian Cycle by Estrogen. W. E. Brown, J. T. Bradbury and A. F. Jennings.—p. 453.

Effect of Low Dosage Roentgen Radiation on Gonadotropic Function of Hypophysis of Mature and Immature Female Albino Rat. J. H. Freed, E. J. Farris, D. P. Murphy and E. P. Pendergrass.—p. 461.

Myxedema with Delayed Closure of Epiphyses in Sexually Mature Women. J. C. M. Fournier, J. C. Barsantini and H. C. Bazzano. —p. 482.

Urinary 17-Ketosteroid Levels of Human Leukemic Subjects. L. Levin. —p. 487.

8:499-636 (July) 1948

*Adrenal Cortical Tumor Associated with Cushing's Syndrome: Report of Case with Metabolic Studies and Remarks on Pathogenesis of Cushing's Syndrome. E. J. Kepler, R. G. Sprague, O. T. Clagett and others.—p. 499.

*Thyrotoxicosis Factitia (Alimentary Thyrotoxicosis): Its Differentiation from Spontaneous Thyrotoxicosis with Aid of Radioactive Iodine. B. N. Skanse and D. S. Riggs.—p. 532.

Hormonal Factors Involved in Regulation of Basal Body Temperature During Menstrual Cycle and Pregnancy. C. L. Buxton and W. B. Atkinson.—p. 544.

Cause of Physiologic Basal Temperature Changes in Women. M. E. Davis and N. W. Fugo.—p. 550.

Fluorometric Method for Clinical Determination of Estrone and Estradiol. J. W. Jailer.—p. 564.

Metabolic Studies in Cushing's Syndrome.—Kepler and his co-workers report a case of adrenal cortical tumor associated with Cushing's syndrome in a woman aged 26. The patient presented hypertension and "hypokalemic," hypochloremic alkalosis. Urinary excretion of both 17-ketosteroids and estrogenic substances was increased to abnormally high levels. Remission of the symptoms followed the removal of the tumor. Recurrence of the tumor was accompanied by the reappearance of the clinical picture. Removal of the recurrent tumor was followed by a temporary and incomplete remission of symptoms. Recurrence of the tumor and the appearance of metastatic lesions in the lungs were associated with the symptoms that were present prior to the removal of the tumor. Roentgen therapy was ineffective. Necropsy revealed that the anterior lobe of the pituitary contained two small chromophobe tumors; Crooke's changes were observed to be present in the basophilic cells of the anterior lobe. The hypothalamus appeared normal. The tumor had recurred locally and had metastasized to the lungs. The contralateral adrenal cortex was atrophic. Metabolic studies were conducted before the first operation and shortly thereafter. Under the conditions employed, the over-all nitrogen balance before operation was negative. Creatinine was present in the urine. Potassium was lost from the body and sodium was retained when the potassium content of the diet was kept at a low level. Administration of potassium chloride tended to correct the alkalosis, the negative balances for potassium and nitrogen and the positive balance for sodium. After removal of the tumor, nitrogen, sodium, potassium and chloride all were retained in large amounts, and creatinuria practically disappeared. The amount and p_H of the urine decreased postoperatively. The metabolic data suggested that the functioning adrenal tumor caused loss of muscle and deposition of fat and that its removal was followed by loss of fat and deposition of muscle. The question of the adrenal versus the pituitary theory of Cushing's syndrome is still open. If the condition is characterized regularly by a high concentration of adrenotropic substance in the blood and urine, one might well conclude that among the endocrine organs the anterior lobe of the pituitary body is primarily at fault. If the administration of adrenal steroids which affect the metabolism of protein and carbohydrate, should be followed in experimental animals by the appearance of Crooke's changes or basophilic tumors or both in the anterior lobe of the pituitary body, it would seem that the adrenal cortices are primarily at fault and that the pituitary abnormalities are secondary and could be ignored therapeutically.

Factitial Thyrotoxicosis.—Skanse and Riggs report a case of factitial thyrotoxicosis in a woman aged 37 in whom hyperthyroidism developed due to clandestine ingestion of thyroid, and a second case in a woman aged 40 in whom circumstantial evidence strongly favored the same diagnosis. In both patients the clinical picture was indistinguishable from that of endogenous thyrotoxicosis. The differential diagnosis was facilitated by the use of tracer doses of radioactive iodine. In endogenous thyrotoxicosis the urinary excretion of radioactive iodine is low compared to that of euthyroid persons. In factitial thyrotoxicosis the excretion of radioactive iodine is higher than normal. Since the serum protein-bound iodine is elevated independently of the source of iodine-containing hormone, this test is not contributory to the differential diagnosis. The combination of an elevated serum protein-bound iodine and high urinary excretion of radioactive iodine is characteristic of, but is not by itself pathognomonic of, alimentary thyrotoxicosis. In a patient with endogenous thyrotoxicosis treated with either thiouracil or iodide one may find the same laboratory pattern until the disease is brought under control. Previous cholecystograms might be responsible for the fact that thyrotoxic patients occasionally have a high excretion of radioactive iodine.

Journal Industrial Hygiene & Toxicology, Baltimore

30:211-264 (July) 1948

Measurement of Alpha-Active Dust in Atmosphere. H. Carmichael and P. R. Tunnicliffe.—p. 211.

*Skin Lesions in Persons Exposed to Beryllium Compounds. R. S. Grier, P. Nash and D. G. Freiman.—p. 228.

Aerobacter Cloacae Endotoxin as Possible Factor in Etiology of Bagassosis. R. Schneiter, W. H. Reinhart and Barbara H. Caminita.—p. 238.

Apparatus for Dispensing Aluminum Dust in Treatment of Silicotics. F. W. Church and F. R. Ingram.—p. 246.

Effects of Physical Characteristics of Fabrics on Physiologic Heat Load and Subjective Reactions. W. R. Christensen.—p. 251.

Penetration of Lead Through Skin. E. P. Laug and Frieda M. Kunze. —p. 256.

Skin Lesions Caused by Beryllium Compounds.—The following types of cutaneous lesions have been observed in those who came in contact with beryllium compounds: contact dermatitis, ulcer of the skin and lesions arising spontaneously in patients with the chronic type of pulmonary disease. To these should be added subcutaneous granuloma occurring in persons who cut themselves on fluorescent lamps coated with beryllium-containing phosphor. The first of the 3 cases reported by Grier and his associates was of a boy, aged 12, who was cut on the side of the neck when he hit an old fluorescent lamp. The other 2 cases concerned men who worked in fluorescent lamp factories and who were accidentally cut with a piece of a lamp. The subcutaneous granulomas which developed in these 3 patients represent distinct form of tissue reaction to beryllium. Pathologically, these granulomas are similar to that seen in the cutaneous lesions which have arisen in the course of the pulmonary granulomatosis caused by beryllium. A similar epithelioid cell reaction has also been found in the lungs of workers who have died of pulmonary granulomatosis following exposure to beryllium compounds. In such cases beryllium has been detected spectroscopically in amounts of the same order of magnitude as was found in the subcutaneous granuloma of case 1. The histology of these granulomas may resemble cutaneous and subcutaneous sarcoidosis so closely that, in some instances, the diagnosis may be missed without a history of exposure to beryllium or determination of beryllium in the tissue. Usually, however, the lesions associated with beryllium show foci of necrosis of a type not seen in sarcoidosis, and the laminated inclusion bodies seem to occur in the former with greater frequency. The incidence of subcutaneous granulomas among those who cut themselves on these lamps is not known, but by analogy with pulmonary granulomatosis, which in one series occurred in 6 per cent of those exposed, it seems likely that in only a few such persons will granulomas develop.

Journal-Lancet, Minneapolis

68:259-296 (July) 1948

Tendon Graft Replacement of Finger Flexors. R. E. Van Demark. —p. 259.
Analysis by Decades of Morbidity and Mortality Trends in Northwest Central Area: One Year's Report of Autopsy Findings (June 1, 1946 to May 31, 1947). G. Berdez and J. J. McLeod Jr.—p. 262.
Study of 1946 Poliomyelitis Epidemic by New Bacteriologic Methods. E. C. Rosenow.—p. 265.
Causes of Error in Proctologic Diagnosis and Treatment. W. A. Fansler.—p. 278.
Streptomycin in Treatment of Various Tuberculous Conditions: Report on Its Use in Minneapolis Veterans Administration Hospital. W. B. Tucker.—p. 282.

Journal National Malaria Society, Columbia, S. C.

7:85-166 (June) 1948. **Partial Index**

Ronald Ross as Medical Discoverer and Poet. R. L. Mégroz.—p. 85.
Temporary Dewatering in Applying Deepening and Filling to Permanently Eliminate Mosquito Breeding Areas in Tennessee Valley Authority Impounded Reservoirs. B. R. Simms and C. C. Kiker. —p. 100.
Duration of Immunity to Malaria (Plasmodium Cathemerium) in Canary. W. D. Gingrich.—p. 109.
Reactions Observed During Treatment with Pentaquine, Administered with Quinacrine (Atabrine), Metachloridine (SN-11,437) and with Sulfadiazine. J. A. Atchley, E. H. Yount, J. R. Husted and others. —p. 118.
Studies on Imported Malarias. D. E. Eyles, M. D. Young and R. W. Burgess.—p. 125.
Observations on Duration of Toxicity of DDT to Anopheles Quadrimaculatus Say Under Field Conditions. A. A. Weathersbee. F. T. Arnold Jr. and J. P. Hopkins.—p. 138.
Effect of One Plant Extract and of Certain Drugs on Development of Plasmodium Gallinaceum in Aedes Aegypti. H. A. Johnson and H. Akins.—p. 144.

Journal of Nervous and Mental Disease, New York

108:1-90 (July) 1948

Psychiatric Aspects of Spontaneous Hypoglycemia. Margaret Bass and P. L. Giovacchini.—p. 1.
Effect Syndrome and Low Back Pain. J. C. Moloney.—p. 10.
*Aldarsone and Bismuth Combined in Treatment of Neurosyphilis: Report of One Hundred Cases. H. Eisenberg and A. S. Hershfield. —p. 25.
*Herniated Disk Simulating Cord Tumor. F. Kennedy, B. Hyde and S. Kaufman.—p. 32.
Clinical Studies of Psychoses in Navy: I. Predication Values of Social Histories and Harrower-Erickson Test. C. K. Aldrich and Mabel Coffin.—p. 36.
Spinal Fluid Sugar in Subarachnoid Hemorrhage. M. J. Madonick and N. Savitsky.—p. 45.
Psychotic Reactions Among Soldiers of World War II. S. Paster.—p. 54.
Painful Hemiplegia Consideration of Central Pain. A. Gordon.—p. 67.

Phenarsone Sulfoxylate and Bismuth in Neurosyphilis.—Eisenberg and Hershfield report on the new pentavalent arsenical, phenarsone sulfoxylate ("aldarsone") in the treatment of neurosyphilis in patients who had previously received various types of treatment, including long term chemotherapy, fever and penicillin, without improvement in their symptoms and spinal fluid findings. All these patients, because of physical contraindications and other reasons, were unable to receive the benefits of further fever therapy. The authors say that 100 patients with various types of neurosyphilis received 2,400 injections of phenarsone sulfoxylate and bismuth compound, concurrently, 1 Gm. of phenarsone sulfoxylate and 1 cc. of bismuth salicylate (2 Gm., equivalent to 75 mm. metallic bismuth). Both drugs were given over a period of twenty-four weeks, once a week, without interruptions. There were 41 cases of asymptomatic and 59 cases of symptomatic neurosyphilis. The Eagle-Wassermann reactions became negative in the spinal fluid in 12 of the 100 patients, and an additional 58 showed a reduction in titer of the Eagle-Wassermann reactions. Fifteen of the patients showed a negative colloidal gold curve and 51 others showed a decrease in the colloidal gold curve. No toxic reactions were noted in any of the cases during or after the treatment. The authors conclude that the concurrent administration of phenarsone sulfoxylate and bismuth is a safe ambulatory treatment of neurosyphilis.

Herniated Disk Simulating Cord Tumor.—Kennedy and his associates direct attention to the fact that herniated nucleus pulposus may simulate a tumor of the spinal cord. They report 3 patients with clinical features of a cord tumor, but operation revealed a herniated nucleus pulposus. In the first and second of the 3 patients the preoperative diagnosis was tumor of the cauda equina. Nothing in the history of the first patient suggested the possibility of a herniated nucleus pulposus. In the second case a review of the history should have suggested the correct diagnosis. The patient had pain, weakness, sensory and reflex changes which vanished in a month, only to return about one year later. In the third case the diagnosis was the same preoperatively and postoperatively, although tumor of the cord had to be seriously considered. The history of intermittent pain for five years suggested the possibility of a herniated nucleus pulposus which may have been partially and intermittently extruded.

J. Neuropathology & Exper. Neurology, Baltimore

7:235-348 (July) 1948

Chronic Experimental Allergic Encephalomyelitis in Monkeys. A. Ferraro and C. L. Cazzullo.—p. 235.
Alterations in Structure of Nerves Caused by Restricting Their Growth with Ligatures. D. Duncan.—p. 261.
Pyridoxine and Pantothenic Acid Deficiency in Swine. R. L. Swank and R. D. Adams.—p. 274.
Granuloblastoma, Primary Neuroectodermal Tumor of Cerebellum. Andrea Saccone and J. A. Epstein.—p. 287.
Angioblastic Neoplasms of Brain. E. W. Corradine and J. Browder. —p. 299.
Experimental Allergic Encephalomyelitis. G. A. Jervis and H. Koprowski.—p. 309.
Posttraumatic Cerebral Swelling Resulting in Cyst Formation. I. M. Scheinker and L. H. Segerberg.—p. 321.
Relation of Changes in Brain to Those in Skull of Crouzon's and Similar Diseases; with Report of Case. Dorothy Eshbaugh.—p. 328.

Journal of Pediatrics, St. Louis

33:1-140 (July) 1948

Effect of Oral Feeding at Different Levels on Absorption of Foodstuffs in Infantile Diarrhea. A. W. Chung.—p. 1.
Effect of Early Oral Feeding Versus Early Oral Starvation on Course of Infantile Diarrhea. A. W. Chung and B. Víšcorová.—p. 14.
Simple Formula for Premature and Full-Term Infants. F. H. Adams. —p. 23.
*Prospects for Prevention of Chronic Bronchitis and Bronchiectasis: Rational Management of Bronchopulmonary Infections by Penicillin Aerosol Therapy. W. Finke.—p. 29.
*Early Whooping Cough Immunization. S. R. Halpern and Doris Halpern.—p. 43.
Heart Disease in San Francisco School Children: 1947 Registry Showing Incidence, Problems, and Supervision Technics. S. J. Robinson, Dorothy M. Aggeler and Gladys Taylor Dariloff.—p. 49.
Further Experience with Hypoxia Tolerance Test of Heart in Children. E. Mannheimer, L. E. Carlgren and W. Graf.—p. 58.
*Congenital Toxoplasmosis. J. Schwartzman, A. Maffia, Margaret E. Crusius and A. Brunhoffer.—p. 66.
Treatment of Tuberculous Meningitis. L. Alperin and J. A. Toomey. —p. 74.
Importance of Pediatric and Surgical Care in Prevention of Selective Service Rejections. W. H. Davis, Jr. and J. M. Arena.—p. 85.

Prevention of Chronic Bronchitis and Bronchiectasis.—A follow-up by Finke on 50 children between the ages of 2 and 15 who were hospitalized in 1945 for bronchopneumonia and treated with sulfonamide drugs and/or parenteral penicillin revealed that 16 of the patients presented symptoms and frequently definite signs of subacute or chronic bronchopulmonary infection two years later. About half of these 16 children had sought medical advice during these two years or had been hospitalized for more severe relapses. Twenty-four others of the 50 children had been affected since their hospitalization in 1945 by relatively mild but recurrent respiratory episodes diagnosed as grip and cold. Thus, only 10 children of the whole group had remained free from respiratory symptoms during the two years following their bronchopneumonia. These observations indicate the potentially recurrent and chronic character of a condition generally misinterpreted as an acute illness. The prospects for prevention of chronic bronchitis and bronchiectasis depend largely on recognition and eradication of the initial bronchopulmonary infection at the earliest possible stage. Penicillin aerosol treatment seems the best available method for achieving the latter. Observations on 15 children with subacute and chronic bronchopulmonary infection treated with penicillin aerosol showed that in patients with early infection the respiratory symptoms usually subsided within a week. Clinical findings indicative of tracheobronchitis disappeared after one to two weeks' treatment; resolution of a subacute bronchopneumonic process took place in one to two months. With continued treatment the accomplished improvement of both the respiratory

infection and the general condition became more and more obvious. The follow-up method used in rheumatic fever and tuberculosis should be applied also to children with potential bronchiectasis in order to give undelayed treatment in the case of a relapse, before it adds new damage to the respiratory system. The prognosis for arrest of definitely chronic cases by penicillin aerosol therapy is less favorable, but encouraging results have been obtained by this new method even in children with pulmonary fibrosis and emphysema.

Early Whooping Cough Immunization.—The Halperns used whooping cough immunization with an alum-precipitated vaccine containing 40 billion organisms per cubic centimeter given in doses of 0.2 cc., 0.3 cc. and 0.5 cc. at monthly intervals in 175 infants of one month of age or less. The first 117 infants receiving skin and agglutination tests prior to the first injection of whooping cough vaccine served as controls. All infants had the skin and agglutination test performed three to four months after the last whooping cough injection. The use of the alum-precipitated vaccine proved to be an effective immunologic procedure as judged by clinical, serologic and skin tests. Reactions were minimal and absences uncommon. If the proper technic is used in administering the vaccine, abscess can be eliminated. The agglutinogen skin test and the rapid slide agglutination method showed a high degree of correlation. The skin test is a simple, reliable and effective method for determining immunity following immunization against pertussis.

Congenital Toxoplasmosis. — Schwartzman and his coworkers report a case of congenital toxoplasmosis in a 17 month old Negro girl. Microcephalus, chorioretinitis, diffuse cerebral calcification and mental deficiency were present. Dwarfism was noted for the first time in this condition. Blood was obtained for inoculation into mice and rabbits, but no toxoplasma was found. Spinal fluid was also injected into these animals, but again no evidence of the parasite was detected. Reactions to neutralizing antibody tests done on the infant's blood were negative. In late cases toxoplasma may not be isolated, and a negative reaction to a neutralizing antibody test after the fourth week of illness does not nullify the diagnosis. Since cases of toxoplasmosis arise as a result of placental transmission, prophylaxis would depend on the early diagnosis of the condition in the pregnant mother. The problem presenting itself is that of devising a simple diagnostic test and also of securing an effective therapy to eliminate the infection before it has produced permanent changes. The discovery of toxoplasma as a cause of mental deficiency and encephalomyelitis adds another causative agent to be considered in these conditions.

Maine Medical Association Journal, Portland

39:143-186 (June) 1948

Treatment of Acute Complications of Diabetes. G. G. Duncan.—p. 143.
Resection of Vagus Nerves in Treatment of Peptic Ulcer. S. F. Fox. —p. 149.

39:187-216 (July) 1948

The Old and the New in Medicine. S. A. Cobb.—p. 187.
The Psychosomatic Patient. M. E. Witte.—p. 190.
*New Ideas on Skin Tests for Food Allergies: Abuses of These Tests in Skin Diseases. L. Babalian.—p. 194.
"Intra-Abdominal Hemorrhage from Rupture by Pregnancy, in Stump of Amputated Fallopian Tube." A. A. Morrison.—p. 196.

Abuse of Skin Tests in Food Allergies.—Babalian shows that the technic of scratch or intradermal tests for food allergies is based on questionable hypotheses. He discusses some of these hypotheses and shows that neither in eczematous dermatitis nor in urticarial lesions are intradermal tests of value in detecting food allergy. As a result of the mistaken confidence in these tests, disorders have been mistakenly regarded as due to food allergy, when they were due either to malnutrition, infection or contact dermatitis. Confidence in skin tests for food allergy has had the unfortunate result that food allergies are regarded as common, which in reality they are not; they are rare in adults and children after the sixth year. Skin tests are of value in other forms of allergy. The importance of contact dermatitis is recognized more and more. Many eczemas formerly regarded as caused by food are now recognized as contact dermatitis.

Medical Annals of District of Columbia, Washington

17:371-428 (July) 1948

*Operative Treatment of Acute Subdeltoid Bursitis with Calcification. P. O. Pelland and W. Hoffman.—p. 371.
Needle Biopsy of Liver: Its Value in Clinical Medicine. I. B. Brick. —p. 377.
Use of Vaginal Cream Containing 9-Aminoacridine in Treatment of Mycotic Vaginitis. L. V. Dill and Shirley S. Martin.—p. 389.
Nitrogen Mustard Therapy of Lymphosarcoma: Report of Case. F. J. Eichenlaub and Matthew A. Olivo.—p. 391.
Use of Methyl-iso-octenylamine (Octin) in Migraine and Related Headaches: Preliminary Report. A. Seltzer.—p. 395.

Subdeltoid Bursitis with Calcification. — Pelland and Hoffman advocate the surgical approach to the treatment of acute subdeltoid bursitis with calcification. The procedure employed is extremely simple, rapid and dramatic in its effect, has not been followed by recurrence and appears to avoid the development of chronicity which occasionally occurs with other methods. It consists in (1) the evacuation of the bursa through an incision not more than 3 cm. long and frequently less, and (2) the exploration of the musculotendinous rotator cuff of the shoulder through the floor of the bursa. The presence of pains and the roentgenologic demonstration of a calcification in the shoulder region are essential indications for this operation. The authors performed it in 38 cases, in 36 of which it produced complete relief. In 1 of the two failures a second operation was successful. It was performed to evacuate a calcific deposit which had been missed previously.

Minnesota Medicine, St. Paul

31:609-720 (June) 1948

Management of Rheumatic Fever and Rheumatic Heart Disease. B. F. Massell.—p. 633.
Abdominal Hodgkin's Disease with Report of Case Involving Retroperitoneal Nodes. W. O. B. Nelson and L. A. Dwinnell.—p. 647.
Clinical Significance of Gross Hematuria. L. F. Greene.—p. 651.
Experiences in Treatment of Volvulus of Sigmoid. C. E. Rea.—p. 653.
Experimental Studies of Liver and Thoracic Duct Lymph. J. H. Grindlay, J. C. Cain, J. L. Bollman and Eunice V. Flock.—p. 654.

Missouri State Medical Assn. Journal, St. Louis

45:465-552 (July) 1948

New Horizons in Medicine. E. L. Bortz.—p. 481.
Medicine Today. R. Mueller.—p. 484.
Diffuse Arteriolar Disease. H. O. Lloyd.—p. 486.
Psychiatric Aspects of Carcinoma of Pancreas. G. Ulett and E. H. Parsons.—p. 490.
Digitalis. T. S. Fleming.—p. 493.

45:553-624 (Aug.) 1948

Sprains. G. Pipkin.—p. 569.
Electric Convulsive Therapy in Mental Disorders Associated with Childbearing. D. A. Boyd Jr. and DeW. W. Brown.—p. 573.
Sequelae of Military Service and Their Treatment in Veterans Administration Mental Hygiene Clinic. N. Blackman.—p. 579.
Electroshock Therapy in Depressions: Notes on Clinical Application. E. H. Parsons and A. B. Scheibel.—p. 583.
Acute Volvulus of the Stomach with Spontaneous Reduction: Report of Case. C. A. Zimmermann III.—p. 585.
Caudal Analgesia: Its Application and Details of Technic. W. H. Masters.—p. 592.
Nephritis: Report of 2 Unusual Cases. R. S. Casford.—p. 599.

New England Journal of Medicine, Boston

239:75-106 (July 15) 1948

*Excessive Hypertension of Long Duration. A. M. Burgess.—p. 75.
Economics of Infant and Child Nutrition. N. B. Talbot, C. C. Koo, W. W. Pick and others.—p. 79.
Physiology. H. E. Hoff and H. J. Scott.—p. 89.
Carcinoma of Gall Bladder. Cholelithiasis.—p. 95.
Duplication of Intestinal Tract (Terminal Ileum).—p. 97.

Excessive Hypertension of Long Duration. — Burgess points out that no previously reported studies have attempted to separate the obviously nonprogressive type of hypertension from the obviously malignant type, and to study the prognosis in the nonmalignant group. With a view to finding out what happens to patients with excessive hypertension that is not of the progressive, malignant type, patients were chosen in whom the condition had existed for at least eight years. In the group of 100 patients here reported a systolic pressure of 180 or a diastolic pressure of 100 was regarded as evidence of excessive hypertension. It was found that hypertension even of an excessive degree, that has been present eight years or more and is not

associated with cardiac or renal disease, usually does not indicate a poor prognosis. The patient usually lives to within three or four years of his normal life expectancy. Such hypertension does not commonly develop into the malignant type. It is not associated with great arteriolar changes, evidenced by retinal hemorrhages or edema, or with renal damage—findings that are typical of malignant hypertension. The most frequent cause of death in these patients is cardiac failure. A cerebrovascular lesion is the most common terminal event. The younger the patient at the time when the hypertension develops, the less likely he is to live his full life span. Even in the young group (age 50 and below) the average length of life is over 15 years (about eleven years below their expectancy). This is the age group in which dorsolumbar sympathectomy is usually recommended. For the malignant type of hypertension this operation is certainly of great value in delaying the fatal issue. With fifteen years or more of life ahead of him, it is questionable whether a person with the nonprogressive, nonmalignant type of high blood pressure should be subjected to such a radical procedure. The degree of hypertension is important in relation to the diastolic pressure only. Persons with extremely high systolic pressures and relatively low diastolic pressures (the arteriosclerotic type of hypertension) survive appreciably nearer to their normal expectancy, on the average, than those with high diastolic pressures.

239:107-158 (July 22) 1948

Value of Antibiotics in Diabetic Surgery. M. J. Kuffel, L. N. Irvin, D. H. Hooker and D. P. Foster.—p. 107.
Addison's Disease Complicated by Chronic Glomerulonephritis. L. Ravreby and W. H. Sawyer.—p. 110.
Spasm and Fibrosis of Sphincter Ani Due to Reflex Action. F. C. Newton and Charles A. Maggregor.—p. 113.
Succinate Therapy in Acute Rheumatic Fever. R. Wégria, E. E. Fischel and P. E. Wilson.—p. 117.
Physiology. H. E. Hoff and H. J. Scott.—p. 120.
Adenocarcinoma of Duodenum at Ampulla of Vater.—p. 145.
Pancreatic Fibrosis.—p. 148.

239:159-212 (July 29) 1948

Report to the New England Surgical Society Concerning the American Board of Surgery. S. C. Harvey.—p. 159.
Rapid Injection of Solution of Amino Acid: Note on Its Clinical Tolerance in Man. R. D. Eckhardt and C. S. Davidson.—p. 164.
Age Distribution of Poliomyelitis in Massachusetts. R. J. M. Horton and A. D. Rubenstein.—p. 169.
*Splenic Rupture in Infectious Mononucleosis. J. J. Timmes, J. H. Averill and J. Metcalfe.—p. 173.
Physiology. H. E Hoff and H. J. Scott.—p. 176.
Retroperitoneal Fibrosarcoma, with Pressure on Right Kidney, Extension into Inferior Vena Cava, Duodenum and Ascending Colon, and with Metastases to Lung.—p. 203.
Echinococcus Cyst.—p. 205.

Splenic Rupture in Infectious Mononucleosis.—Timmes and his associates report 2 cases of infectious mononucleosis in which splenic rupture occurred. Both cases concerned 19 year old seamen. In the first case the diagnosis was not suspected preoperatively. The history of lymphadenopathy, the strongly positive heterophil antibody agglutination and the splenic disease made the diagnosis extremely probable. In the second case a tentative diagnosis of a subcapsular splenic hemorrhage was made on the basis of persistence of abdominal findings and the probability of infectious mononucleosis. In both cases the postoperative course was uneventful. The authors review 14 cases of splenic rupture in infectious mononucleosis that have been reported in the literature. They stress that with more general appreciation of the fact that in infectious mononucleosis splenic rupture may occur either spontaneously or as the result of minimal abdominal trauma three things may be accomplished. The performance of diagnostic tests for infectious mononucleosis in patients suspected of splenic rupture, and in the postoperative study of those from whom a ruptured spleen has been removed, may lead to a revision of the present estimate of the rarity of the condition. Secondly, avoidance of heavy exertion during the phase of infectious mononucleosis in which the spleen is enlarged and avoidance of repeated palpation of an enlarged spleen in patients with infectious mononucleosis may lower the incidence of this complication. Careful observation of patients with infectious mononucleosis for evidence of abdominal pain or acute blood loss may lead to more prompt surgical action, with resultant improvement in the mortality figures of this complication.

New Jersey Medical Society Journal, Trenton

45:273-320 (June) 1948

Carcinoma of Gall Bladder: Report of 26 Cases. M. Danzis.—p. 274.
Anthrax of Eyelid. Emilie V. Rundlett.—p. 277.
Use and Misuse of Hormones in Obstetrics and Gynecology. A. E. Rakoff.—p. 278.
Clinical Observations on Scabies. S. A. Klein.—p. 283.
Clinical Evaluation of Liver Function Tests. H. Greenfield.—p. 284.
What Is Cause of Congenital Malformations? W. B. Nevius.—p. 289.

45:321-376 (July) 1948

Problem of Long-Term Patient in New Jersey. E. Frankel.—p. 323.
Prevention of Common Cold. A. Bensel.—p. 328.
Constructive and Destructive Aspects of Atomic Energy. H. H. Lawrence.—p. 330.
*Industrial Sight Conservation Program for New Jersey. H. Weltchek.—p. 335.
Prophylaxis in Postoperative Thrombo-Embolus: Preliminary Report. M. Joseph.—p. 337.

Industrial Sight Conservation.—Weltchek says that proper examination of vision for industrial purposes should include (*a*) vision at 20 feet (6.1 meters), (*b*) vision at approximately 14 inches (35.6 cm.) and (*c*) vision at working distance. The vision at working distance is by far the most important part of the examination. In many instances, vision "at distance" and the vision "at near" do not correspond to vision at working distance. In an industrial procedure where fine or even gross work is done at a distance of 20 inches (50.8 cm.) from the eye, it is useless to test vision for ordinary "near" and to attempt to correct it by the usual correction for near vision; i. e., 14 inches. Proper illumination and eye safety are also important. Five "pilot" studies in various industries throughout New Jersey are now in progress. Factual material is thus being collected for the purpose of improving present concepts and practices of industrial sight conservation.

New Orleans Medical and Surgical Journal

101:1-46 (July) 1948

SYMPOSIUM ON BIOPSY PROCEDURE IN CANCER AND PRECANCEROUS LESIONS

Biopsy in Otolaryngology. G. J. Taquino.—p. 1.
Biopsy in Gastrointestinal Practice. G. McHardy and D. C. Browne.—p. 2.
Biopsy in Dermatology. C. B. Kennedy.—p. 3.
Office Biopsy in Obstetrics and Gynecology. E. L. Zander and E. R. Guidry.—p. 4.
Use of Biopsy in Urologic Practice. W. E. Kittredge.—p. 7.
Biopsy (Proctology). M. Lescale.—p. 9.
New Retractor for Use in Thyroidectomy. H. Mahorner.—p. 10.
Salmonella Blegdam Infection: Review of Literature and Report of Case. J. R. Foster.—p. 11.
Bilateral Brodie's Abscess: Report of Case. E. R. Riggall.—p. 12.
Intratracheal Anesthesia: Its Uses and Abuses. S. R. Mintz and J. Adriani.—p. 16.
Spinal Anesthesia for Cesarean Section. D. A. Roman and J. Adriani.—p. 19.
Use of Histamine Antagonist in Intravenous Pyelography. P. L. Getzoff.—p. 22.
Corneal Transplantation. R. T. Paton.—p. 25.
Dithiopropanol (BAL) in Treatment of Bichloride Poisoning. V. D'Ingianni.—p. 30.
Nitrogen Mustard Therapy. C. B. Luikart and N. S. Gilbert.—p. 32.

North Carolina Medical Journal, Winston-Salem

9:323-366 (July) 1948

The Ego and the Eye. T. A. Watters.—p. 323.
Indications for Nephro-Ureterectomy with Illustrative Cases. H. W. McKay and H. H. Baird.—p. 328.
*Salmonellosis Due to Salmonella Oregon. M. Fulton and H. L. Godwin.—p. 332.
Report of Fourteen-Month Study on Use of Vaginal and Cervical Smears in Diagnosis of Genital Malignancy. J. R. Kernodle, W. K. Cuyler, Mary K. Taylor and Pauline Jones.—p. 335.
*Effect of Anti-Reticular Cytotoxic Serum: Observations on Cases of Hodgkin's Disease. J. W. Abernethy, G. T. Harrell, L. M. Morris, H. L. Valk and others.—p. 341.
Continuous Caudal Analgesia in Poor-Risk Obstetric Patients, Especially Those with Marginal Placenta Praevia. A. T. Thorp.—p. 350.

Salmonellosis Due to Salmonella Oregon.—Fulton and Godwin feel that bacteriologic and serologic studies on patients infected with the rarer types of Salmonella are still needed. They present the case of a farmer, aged 67, who was hospitalized because of diffuse prostatic enlargement. After he had been in the hospital for more than a month, his temperature went up to 102 F. He complained of headache, cramping pain in the lower part of the abdomen and multiple watery stools.

These symptoms were accompanied by occasional bouts of nausea and vomiting. A stool culture yielded Salmonella oregon. This is the first case of Salmonella oregon identified in North Carolina, and the eleventh involving the occurrence of this organism in man. No other cases or carriers of Salmonella were detected in the patient's ward. A five day course of sulfadiazine had no apparent effect, but later the diarrhea ceased. Sulfonamide compounds apparently are not effective, and streptomycin seems to be a more promising agent. However, the mortality rate in cases of salmonellosis is low, and in view of the possibility that the organism may become resistant to streptomycin, it might be wise to hold the drug for use if and when massive invasion or septicemia occurs.

Antireticular Cytotoxic Serum in Hodgkin's Disease.—Abernethy and his associates review observations on 7 cases of Hodgkin's disease in which antireticular cytotoxic serum was administered as an adjunct to irradiation therapy. They studied the effect of the serum on the circulating blood cells, on the rate of tissue destruction, on capillary permeability and on a possible infection with Brucella. Minimal evidence suggestive of transient alteration in the reticuloendothelial system was noted; observed changes in the differential white blood cell count and in the sedimentation rate confirmed the Russian reports. Other alterations in function reported by the Russians were not confirmed, and additional objective tests to supplement the ones which they recorded failed to support their theories. The results from the use of antireticular cytotoxic serum as an adjunct to therapy in Hodgkin's disease have so far been disappointing.

Northwest Medicine, Seattle

47:491-542 (July) 1948

Esophageal Diverticula. R. F. Ahlquist and M. F. Kepl.—p. 493.
Surgical Management of Intrathoracic Esophageal Lesions. R. D. Pinkham.—p. 496.
Resection of Lower Esophagus for Bleeding Varices: Report of Case. D. B. Seabrook.—p. 498.
Unexpected Death of Apparently Healthy Adults from Natural Causes. A. R. Moritz.—p. 500.
Weil's Disease Treated with Penicillin. C. Barron and J. H. Mills. —p. 502.
Scleroma. C. K. Miller.—p. 504.
Use of Cushing Clip in Transabdominal Vagotomy: Unusual Complication. R. R. De Nicola and P. E. Kendall.—p. 505.
Injury to Liver with Biliary Fistula. M. L. Johnson.—p. 508.
Cancer Detection Centers in State of Washington. C. P. Larson.—p. 510.
Mesantoin in Treatment of Epilepsy. N. K. Rickles.—p. 513.
Multiple Sclerosis: Diagnosis, Therapy and Rehabilitation. J. T. Robson. —p. 514.

Occupational Medicine, Chicago

5:1-30 (Jan.) 1948

Value of Early Ambulation in Industrial Surgical Treatment. D. J. Leithauser.—p. 1.
Illness and Injury Rates in Small Industrial Plants: Study in Factory Epidemiology. J. W. Meigs.—p. 11.
*Study of Resuscitation from Juxtalethal Effects of Exposure to Carbon Monoxide. H. Schwerma, A. C. Ivy, H. Friedman and E. La Brosse. —p. 24.
Primary Care of Injured Hand. J. C. Detro.—p. 49.
Study of Lead Exposures in Three Metropolitan Newspaper Plants. J. F. Keppler and H. E. Bumsted.—p. 65.
Effects of New Forms of Energy on Industry and Medical Service. J. S. Felton.—p. 73.
Dislocation of Thyroid Cartilage: Report of Case. E. J. Elsbach.—p. 78.

Resuscitation After Exposure to Carbon Monoxide.—This report by Schwerma and his co-workers presents the results obtained when dogs were exposed in a chamber to air containing 0.3 per cent carbon monoxide from the gas main in Chicago until the first respiratory gasp occurred. At this point the animal was immediately removed from the chamber and one of six procedures was instituted. Thirty-six per cent, or 8 of 22 dogs, survived when given manual artificial respiration in air. Forty-three per cent, or 13 of 30 dogs, survived when given manual artificial respiration in 7 per cent "carbogen." Sixty-nine per cent, or 57 of 82 dogs, survived when given mechanical artificial respiration with a device providing alternating positive and negative pressure, using 100 per cent oxygen. Sixty-six per cent, or 55 of 83 dogs, survived when given mechanical artificial respiration with the same device, using 7 per cent "carbogen." Sixty-five per cent, or 13 of 20 dogs, survived when given mechanical artificial respiration with an alternating positive pressure device, using 100 per cent oxygen. Mechanically produced artificial respiration using 100 per cent oxygen or 7 per cent "carbogen" is significantly superior to that produced manually in air. Regardless of this fact, the manual method must be taught because it is always available. Three cases of pneumonia (10 per cent) occurred among the 31 survivors resuscitated by manual artificial respiration or by being placed in "fresh air." Twenty-six cases of pneumonia occurred among 125 survivors (24 per cent) which were resuscitated with positive pressure devices. This difference is not considered significant, since it could occur by chance in 15 of 100 such experiments. The incidence of pneumonia was the same whether 100 per cent oxygen or 7 per cent "carbogen" was used for resuscitation. In regard to survival and the incidence and severity of neurologic sequelae no difference was found between the use of 100 per cent oxygen and 7 per cent "carbogen" in resuscitation from carbon monoxide asphyxia.

Psychiatry, Washington, D. C.

11:105-222 (May) 1948. **Partial Index**

Towards Psychiatry of Peoples. H. S. Sullivan.—p. 105.
Anti-Nazis: Criteria of Differentiation. D. M. Levy.—p. 125.
Rôle of Parent in Psychotherapy with Children. Hilde Bruch.—p. 169.
Maine, McLennan, and Freud. A. J. Levin.—p. 177.

Public Health Reports, Washington, D. C.

63:901-932 (July 9) 1948

Studies on Duration of Disabling Sickness: VII. Duration Table for Specific Causes of Disability Among Male Workers. W. M. Gafafer. —p. 901.

63:933-966 (July 16) 1948

Bactericidal Properties of Chloramines and Free Chlorine in Water. C. T. Butterfield.—p. 934.
Relation of Reported Cases of Typhus Fever to Location, Temperature, and Precipitation. C. R. Eskey and F. M. Hemphill.—p. 941.

63:967-990 (July 23) 1948

Technic in Evaluation of Rapid Antisyphilitic Therapy. A. P. Iskrant, R. W. Bowman and J. F. Donohue.—p. 965.

63:991-1026 (July 30) 1948

Transfer of Malarial Parasites Between Blood Films During Mass Staining Procedures. M. M. Brooke and A. W. Donaldson.—p. 991.
Combined Typhus-Malaria Control Residual Spray Operations with Five Percent DDT Emulsion. H. P. Nicholson, T. B. Gaines, J. G. McWilliams and M. H. Vetter.—p. 1005.

Surgery, Gynecology and Obstetrics, Chicago

87:129-256 (Aug.) 1948

*Portacaval Shunts in Treatment of Portal Hypertension: Analysis of 15 Cases with Special Reference to Suture Type of End-to-Side Splenorenal Anastomosis with Splenectomy and Preservation of Kidney. R. L. Linton, I. B. Hardy Jr. and W. Volwiler.—p. 129.
Childbearing in Twilight of Reproductive Period. M. E. Davis and A. Seski.—p. 145.
Carcinoma of Lip: Review of 563 Case Records of Carcinoma of Lip at Pondville Hospital. J. E. Cross, E. Guralnick and E. M. Daland. —p. 153.
Blood Volume and Other Determinations in Preoperative and Postoperative Care: Their Practical Applications in Average Hospital. C. A. Beling, T. V. Morton and D. T. Bosch.—p. 163.
*Surgical Aspects of Hyperparathyroidism: Review of 63 Cases. M. Black. —p. 172.
Interatrial Septal Defect—Its Experimental Production Under Direct Vision Without Interruption of Circulation. A. Blalock and C. R. Hanlon.—p. 183.
*Studies on Vagotomy in Treatment of Peptic Ulcer: III. Physiologic Aspect. I. F. Stein Jr. and K. A. Meyer.—p. 188.
*Cervical Cytology: Key to Diagnosis of Early Uterine Cancer. H. Oxorn.—p. 197.
Acute Non-Clostridial Crepitant Cellulitis. W. A. Altemeier and W. R. Culbertson.—p. 206.
Discussion of Uses of Metals in Surgery and Experimental Study of Use of Zirconium. J. I. Bates, C. R. Reiners and R. C. Horn. —p. 213.
Reactions to Morphine in Ambulatory and Bed Patients. J. H. Comroe Jr. and R. D. Dripps.—p. 221.
Re-Evaluation of Role of Pyloric Antrum in Marginal Peptic Ulcers. J. A. Schilling and H. E. Pearse.—p. 225.

Portacaval Shunts in Treatment of Portal Hypertension.—Linton and his associates discuss various types of portal bed block and report observations on 15 patients who have been treated by various types of shunt operations. The most common form of intrahepatic block results from portal or Laennec's

cirrhosis secondary to the scar tissue replacement of the liver parenchyma. The extrahepatic portal bed block (so-called Banti's syndrome) may be either congenital or acquired. A combination of the intrahepatic and extrahepatic types may also occur. It was present in 2 of the 15 cases reviewed by the authors. Patients with portal hypertension secondary to a portal bed block, as a rule, seek medical advice because of a sudden massive hematemesis or melena. Portal hypertension should always be considered in the differential diagnosis of hematemesis or melena. Roentgenologic examination of the esophagus with barium to determine the presence or absence of varices is the most important diagnostic procedure. The portacaval shunt type of operation represents a new chapter in the treatment of portal hypertension. It apparently prevents serious hemorrhage from esophageal varices, although they may still persist, and in addition it may improve the hepatic function. Splenectomy and the suture type of end to side splenorenal anastomosis with preservation of the kidney, performed through a thoracoabdominal incision, are recommended as the most satisfactory operative procedure in cases in which the spleen has not been previously removed. Anastomosis of the superior mesenteric vein to the inferior vena cava and of the inferior mesenteric vein to the left ovarian vein has been utilized with apparent success, in 2 patients who had had the spleen previously removed. Direct anastomosis of the portal vein to the inferior vena cava may frequently be impossible due to the extreme degree of vascularity in the region of the gastrohepatic ligament. The results of various types of portacaval shunts have been more satisfactory in extrahepatic portal bed block than in the intrahepatic type.

Surgical Aspects of Hyperparathyroidism.—Black reports on 63 patients with proved hyperparathyroidism that were observed at the Mayo Clinic to the end of 1946. The disease was due to a single adenoma in 56 cases, to multiple adenomas in 3 cases and to diffuse primary hyperplasia in 4 cases. Complications of the urinary tract were more common and more important than osseous complications. Since the diagnosis can be made with certainty, exploration of the parathyroid glands is never indicated to establish the diagnosis. The treatment of hyperparathyroidism is surgical. Adenomas should be removed completely and, in cases of diffuse primary hyperplasia, the hyperplastic tissue should be excised subtotally, with preservation of 30 to 200 mg. of hyperplastic tissue. In more than 80 per cent of cases, the abnormal tissue may be found by dissection under direct vision through a cervical incision (cervical and posterior superior mediastinal dissection). A second operation, through a sternotomy incision, will be necessary in the remaining cases (anterior superior mediastinal dissection). Secondary dissection is more difficult and far less certain than primary dissection, so that every effort should be made at complete operation, both in identifying the parathyroid glands present and in designating those missing, at the first cervical dissection.

Physiologic Aspects of Vagotomy in Peptic Ulcer.—Stein and Meyer say that in June of 1946 a study of vagotomy in the treatment of peptic ulcer was started on one of the surgical services at the Cook County Hospital. Vagus section was carried out in 35 instances. Physiologic studies of the stomach were made before and after vagotomy in 30 patients. Each of the following determinations was made on a significant number of patients before and after surgery: (1) twelve hour night secretion, (2) basal secretion, (3) the effect of histamine on gastric secretion, (4) the effect of caffeine on gastric secretion, (5) the effect of atropine on basal secretion, (6) the spontaneous motility of the stomach and the effect of insulin on secretion and motility, (7) the pain threshold to electrical stimulation and (8) the production of pain by the introduction of acid into the stomach. The secretory activity of the stomach may be divided into the period of interdigestive or continuous secretion and the digestive period of secretion. The latter consists of three phases: the cephalic, the gastric and the intestinal. The cephalic gastric secretion is mediated entirely by the vagi. The gastric phase can be provoked by mechanical stimulation and secretagogues, and has been considered independent of the vagus. In view of the considerable decrease in the secretory response to histamine and caffeine after complete vagotomy, it is apparent that the gastric phase of secretion is also to some extent influenced by the vagus. The secretory response to chemical stimuli was reduced in every patient in whom the insulin test indicated that vagotomy was complete. The authors feel that the inconsistent results reported by other workers may be due to failure to distinguish between completely and incompletely vagotomized subjects. They also obtained confirmatory evidence of the reliability of the insulin test as an indication of the completeness of vagotomy. After complete vagotomy there is a considerable reduction of the night secretion and the basal secretion. The secretory response of the stomach to caffeine and histamine is greatly reduced. There are no spontaneous hunger contractions in the fundus of the stomach up to nine months after complete vagotomy. Complete vagus section in some manner interrupts a mechanism necessary for chronicity of peptic ulceration.

Cervical Cytology in Early Uterine Cancer.—Oxorn discusses the basic principles of the cytologic tests and their application in the early diagnosis of cancer of the uterus. He describes the vaginal aspiration, the cervical aspiration and the cervical spatula technic and discusses their relative merits. It is believed that the cervical spatula test is the most efficient in the diagnosis of extremely early cervical cancer. Emphasis is placed on the importance of having a central laboratory in each district where expert study of these smears may be made. Describing the glycerine mailing technic of Ayre and Dakin, the author says that after standing in the ether-alcohol fixer for one hour, or more, the slides are removed from the solution. Without permitting them to dry, one places a large drop of glycerine in the center of the secretion zone. A second, clean, slide is placed face to face with the smear, and the glycerine spreads out to cover the entire smear area, sealing it off completely. Each unit is made up of two slides: (1) the slide with the smear on it and (2) a clean slide acting as a cover slip. The slides are then placed in wooden or cardboard containers, to prevent breakage, and are mailed to the cytology laboratory. Once the slides arrive at their destination the glycerine is washed off, and the usual staining routine is carried out. Smears can be taken by every practitioner in his office. This combined with the mailing technic makes it possible for every doctor and every patient to reap the benefits of this modern diagnostic procedure. Cancer of the uterine fundus as well as cancer of the cervix can be diagnosed accurately by the cytology method. These smears provide a reasonably accurate measure of endogenous body estrogen at any one time. The advantages and disadvantages of the tests are presented. It is concluded that the use of routine periodic check-ups with cytologic tests at each visit will do much to lower the present high mortality rate from uterine cancer.

Texas State Journal of Medicine, Fort Worth

44:67-188 (June) 1948

Blueprint for Action. B. E. Pickett.—p. 73.
Memorial Address. J. W. Torbett Sr.—p. 77.
Medical Legislation. G. F. Lull.—p. 78.
Present Status of Synergistic and Additive Chemotherapy. J. A. Kolmer.—p. 81.
Your Health and the Soil. E. P. McKinney.—p. 85.

44:189-276 (July) 1948

Relation of General Practitioner to Over-All Health Program. W. M. Johnson.—p. 192.
It's Health Roundup Time in Texas. H. Emerson.—p. 195.
Responsibilities and Duties of Federal, State, and Local Health Agencies. J. W. Bass.—p. 199.
Statistical Data in Preventive Medicine and Public Health Administration. L. P. Walter.—p. 203.
Epidemiology and Recent Developments in Poliomyelitis. J. G. Molner.—p. 207.
Tonsillectomy and Poliomyelitis. J. W. Eschenbrenner.—p. 211.
Q Fever: Present Status in United States. E. Strauss and S. E. Sulkin.—p. 214.
Tuberculosis Eradication—a Possibility. E. Mendenhall.—p. 218.
Present Status of Pediatric Care in Texas. D. Greer.—p. 221.

West Virginia Medical Journal, Charleston

44:177-208 (July) 1948

West Virginia University and Medical Education in West Virginia. I. Stewart.—p. 177.
Diet and Insulin in Some Diabetic Complications. G. P. Heffner.—p. 185.
Intervertebral Disk Lesions. J. M. Meredith.—p. 191.
Cardiac Emergencies. S. M. Jacobson.—p. 197.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Annals of Rheumatic Diseases, London

7:63-126 (June) 1948

Necrobiotic Nodules of Rheumatoid Arthritis: Case in Which Scalp, Abdominal Wall (Involving Striped Muscle), Larynx, Pericardium (Involving Myocardium), Pleurae (Involving Lungs), and Peritoneum Were Affected. R. W. Raven, F. P. Weber and L. W. Price.—p. 63.
*Investigations into Effect of Hot, Dry Microclimate on Peripheral Circulation, etc., in Arthritic Patients. G. Edström, G. Lundin and T. Wramner.—p. 76.
Flocculation Tests in Rheumatoid Arthritis. T. N. Fraser.—p. 83.
Interstitial Neuritis and Neural Theory of Fibrositis. M. Kelly.—p. 89.
Relation of Cardiac Lesions of Rheumatoid Arthritis to Those of Rheumatic Fever. A. D. Wallis.—p. 97.
Controlled Series of Cooke-Arneth Polynuclear Counts in Rheumatoid Arthritis. H. J. Gibson and D. Shiers.—p. 100.
Phosphatase Activity in Spondylitis Ankylopoietica. M. H. L. Desmarais. —p. 105.

Hot, Dry Climate for Arthritic Patients.—For the last six years Edström and his associates have had one ward in the rheumatologic department of the University Hospital in Lund constantly air conditioned at 32 C. and 35 per cent relative humidity. In this ward they have treated arthritic patients, each of them for about a hundred days. The peripheral circulation increased in all. Peripheral vasospasm was converted into peripheral vasodilatation. The arteriovenous anastomoses especially have been maximally dilated. The temperature of the skin, which was lower at an ordinary room temperature of 20 C. (especially in cases of rheumatoid arthritis) has been raised, particularly on hands, feet and distal part of the extremities. The relative oxygen saturation of venous blood, measured at the medial cubital vein, increased in the hot rooms, while the arteriovenous difference diminished. Cultures from the throat flora showed in most cases beta-hemolytic streptococci on admission of patients to the hot room, but only in 2 cases were such cocci detected at the end of their stay. These cocci apparently do not tolerate this dry hot climate. The most obvious effects on the clinical symptoms have been: remission of periarticular edema and capsular swelling of joints, diminished shifting pains and contractures, better appetite, improved function in cases of cardiac defects and disappearance of the blue livid coloration of skin on hands and feet. Tendency to recurrence immediately after removal back into ordinary room temperature has not been observed.

British Heart Journal, London

10:1-64 (Jan.) 1948

Angina in Women. V. K. Summers.—p. 4.
Clinical Value of Unipolar Chest and Limb Leads. C. W. C. Bain and E. McV. Redfern.—p. 9.
*Two Cases of Temporal Arteritis: One with Angina of Effort. L. Cole. —p. 26.
Hypertension Due to Syphilitic Occlusion of Main Renal Arteries. R. K. Price and R. Skelton.—p. 29.
Ball Thrombus of Heart. M. E. Evans.—p. 34.
Mass Thrombus of Left Auricle. W. Evans and R. Benson.—p. 39.
Variation of Casual, Basal, and Supplemental Blood Pressures in Health and in Essential Hypertension. J. A. Kilpatrick.—p. 48.
Cardiovascular Changes Following Electro-Convulsive Therapy. R. Kauntze and G. Parsons-Smith.—p. 57.

Temporal Arteritis.—The age of onset in Cole's 3 patients was between 65 and 72, and the symptoms and signs produced by involvement of the temporal arteries ran a course lasting from four to six months. All 3 showed evidence of arteriosclerosis in the radial and brachial arteries, and 2 died suddenly from cardiovascular accidents. The key to the diagnosis has been severe headaches leading to the discovery of the involvement of the temporal arteries. More cases should be published in order that the condition may be widely recognized and more may be learned about its protean manifestations. At present the general verdict is that the prognosis is good as far as the local condition in the temporal arteries is concerned, for this tends to clear up in about a year. It is not yet so clear how far extension of the process to more vital arteries may be responsible for deaths such as occurred in these patients, and a follow-up of more cases is needed.

British Journal of Dermatology and Syphilis, London

60:195-234 (June) 1948

Psoriasis of Nails. J. Alkiewicz.—p. 195.
Pityriasis Rosea Sparing Tanned Areas of Skin: Report of 2 Cases. J. Kinnear.—p. 200.
Erythrosis Pigmentosa Peribuccalis. E. L. Cohen.—p. 203.
Report on Case of Leukemia Cutis. H. D. Chambers.—p. 211.

British Journal of Experimental Pathology, London

29:93-190 (April) 1948

Prolonged Administration of Thyroxine to Cows, with Particular Reference to Effects on Thyroid Function and on Pituitary Thyrotrophic Hormone. M. T. McQuillan, V. M. Trikojus, A. D. Campbell and A. W. Turner.—p. 93.
Rift Valley Fever: Isolation of Virus from Wild Mosquitoes. K. C. Smithburn, A. J. Haddow and J. D. Gillett.—p. 107.
Bodily Reactions to Trauma: Effect of Ischemia on Muscle Protein. H. B. Stoner and H. N. Green.—p. 121.
Influenza in Great Britain 1946-47. J. A. Dudgeon, H. Mellanby, R. E. Gloyer and C. H. Andrewes.—p. 132.
Antigenic Efficiency of CL. Welchii Epsilon Toxin and Toxoid After Treatment with Trypsin. I. Batty and A. T. Glenny.—p. 141.
*Effects of Short-Term Changes in Dietary Protein on Response of Liver to Carbon Tetrachloride Injury. R. M. Campbell and H. W. Kosterlitz.—p. 149.
Detection of Product of Blood Group O Gene and Relationship of So-Called O-Substance to Agglutinogens A and B. W. T. J. Morgan and W. M. Watkins.—p. 159.
Fibrin Barrier Regarded as Filter in Inflammation. W. H. Hughes. —p. 173.
Virulence and Toxigenicity of Different Serologic Types of C. Diphtheriae. L. F. Hewitt.—p. 181.

Effects of Short Term Changes in Dietary Protein on Liver in Carbon Tetrachloride Injury.—According to Campbell and Kosterlitz the nutritional condition of an animal greatly determines its resistance to toxic halogenated hydrocarbons. In view of the fact that the protein content of the diet determines the amount of labile cytoplasm (protein plus phospholipin plus nucleic acid, PPN) present in the liver cell it was of interest to examine whether the severity of liver injury caused by a single administration of carbon tetrachloride could be correlated with the presence or absence of labile PPN. Rats were placed on a protein-free 18 per cent or 54 per cent casein diet for three days prior to a single injection of carbon tetrachloride. The damage to the liver as measured by central necrosis, hydropic degeneration and deposition of neutral lipids was least on the protein-free diet. The rats on the 18 per cent casein diet showed the highest incidence of hydropic degeneration, and those on the 54 per cent casein diet the greatest deposition of neutral lipids. On all diets there was a considerable loss of glycogen. These results are in agreement with the findings of other observers, that, if given for short periods before the administration of chloroform or carbon tetrachloride, a diet rich in carbohydrate, low in fat and protein gives the highest protection against injury to the liver. On the other hand, prolonged dietary protein deficiency leads to protein depletion, which renders the liver highly susceptible to this type of injury.

British Medical Journal, London

1:1221-1270 (June 26) 1948

*Modern Therapy of Benign Tertian Malaria. J. F. Monk.—p. 1221.
Demonstration of Persisting Exo-Erythrocytic Cycle in Plasmodium Cynomolgi and Its Bearing on Production of Relapses. H. E. Shortt and P. C. C. Garnham.—p. 1225.
Bilharzial Affection of Ureter: Study of 110 Consecutive Necropsies Showing Vesical Bilharziasis. M. Gelfand.—p. 1228.
Recent Trends in Treatment of Prostatic Obstruction. A. Jacobs. —p. 1231.
Lower-Segment Caesarean Section: New Head Extractor. B. C. Murless. —p. 1234.
Papillomata of Bladder Treated with Podophyllin: Preliminary Report. J. E. Semple.—p. 1235.
Case of Sarcoma of Larynx. E. Broughton-Barnes, E. S. Duthie and B. Jolles.—p. 1237.

Modern Therapy of Benign Tertian Malaria.—Monk points out that the recent war gave impetus to the search for the ideal antimalarial drug. He reviews the stage at which the treatment of benign tertian malaria has arrived, discussing experiences with the following drugs: quinine, quinacrine, an acridine dye, "paludrine hydrachloride" (chlorguanide hydrochloride), chloroquine, a 4-aminoquinoline derivative, pamaquine, an 8-aminoquinoline compound, and pentaquine, an 8-aminoquinoline derivative. The ideal drug for the prevention and cure of benign tertian malaria is still to be found. Quinine therapy alone and unaided is of little value. Suppressive and

curative treatment with quinacrine is likely to be superseded by more recently discovered antimalarial drugs. Chlorguanide and chloroquine are probably effective in producing complete suppression of overt attacks of malaria in once-weekly dosage. Neither is able to prevent the establishment of Plasmodium vivax in the human host even by daily dosage, but chlorguanide has some inhibitive effect on the preerythrocytic forms. Neither drug given alone is as successful as other forms of therapy in producing a low relapse rate. Pamaquine is a drug which deserves greater recognition as a safe medium for the elimination of P. vivax infections. Given as an adjuvant in any course of antimalarial therapy, it is of the greatest value in reducing the relapse rate. The toxicity of pamaquine is shown to be less formidable than is generally accepted. No treatment so far administered to a large series of patients with naturally occurring benign tertian malaria is more successful than quinine given concurrently with pamaquine. Chlorguanide given concurrently with pamaquine is equally successful. Pentaquine given concurrently with quinine is likely to prove more successful in producing a lower relapse rate than any other therapeutic regimen. The toxicity of pentaquine is approximately three quarters that of pamaquine. A thirty-one day intermittent course of quinine and pamaquine proved successful in the complete eradication of P. vivax infections in all patients followed up in a series of 45 cases. It is suggested that such a course is worth extended trials among cases of chronic relapsing malaria in a nonmalarious area.

Journal of Mental Science, London

94:215-512 (April) 1948. **Partial Index**

Identity of Alzheimer's Disease and Senile Dementia and Their Relationship to Senility. R. D. Newton.—p. 225.
Genetics in Relation to Mental Disorders. F. J. Kallmann.—p. 250.
Mental Deficiency and Social Medicine. E. O. Lewis.—p. 258.
Modern Approach to Juvenile Delinquency: Observation Centers. A. Kennedy.—p. 283.
Significance of Home for Child's Emotional Development During First Six Years. Kate Friedlander.—p. 305.
Medea Complex: Mother's Homicidal Wishes to Her Child. E. S. Stern.—p. 321.
Physiologic and Psychologic Responses to Stress in Neurotic Patients. M. Jones.—p. 392.
*Personality Change and Prognosis After Leukotomy. G. Garmany.—p. 428.
Delinquency and Epilepsy: Clinical and Electrophysiologic Note. R. S. Hodge.—p. 439.
*Kent and Other Tests Used on Same Subjects. G. De M. Rudolf.—p. 452.
Management of Chronic Mental Patients. A. P. Tait.—p. 459.

Personality Change After Leukotomy.—Garmany reports on 59 patients who had undergone leukotomy not less than three years previously. Leukotomy proved successful in half of the 22 patients with depression and also in half of the 10 patients with paranoid schizophrenia, but in only 1 of 15 patients with hebephrenia and in only 2 of 10 patients with catatonic schizophrenia. The author believes that no permanent personality change occurs which is ascribable to the operation alone. Restitution depends materially on the possibility of rehabilitation, particularly in the patient's own home. In depression, a good personality, free from lifelong morbid patterns of reaction, and average intelligence are essential if a good prognosis is to be given. Heavily emphasized hypochondriacal reactions or *bizarrerie* are bad omens, and equally so are schizophrenic features and organic dementia. In the case of hebephrenic and catatonic reactions, it seems doubtful whether the operation is worth doing unless circumstances are quite exceptional; in paranoid schizophrenia the operation seems to offer reasonable hope if the premorbid personality was good, and particularly if passivity and catatonic features are not prominent. It is well to remember that the curative effects of leukotomy may not be permanent, and the reorganization of disease patterns shown in 3 cases in this series, after a long period of comparative fitness, may prove to be a not uncommon phenomenon with longer observation.

The Kent and Other Tests.—Rudolf points out that tests of the indefinable quality known as intelligence are legion. Many have been standardized satisfactorily; others have not. The validity of some tests is high, but results of different tests used on the same persons have seldom been published. In the comparative investigations reported in this paper a total of 1,566 persons were examined as follows: (1) 557 subjects, each tested with the Kent and the Stanford-Binet tests; (2) 409 subjects, each tested with the Kent and part I of the Farmer-Hotoph 3 (or R) given as a group test, and (3) 600 subjects, each tested with the Kent and the Progressive matrices given as a group test. On the basis of the results obtained, the author concludes that the Kent emergency test cannot be used as an alternative to the Stanford-Binet, the progressive matrices, or the Farmer-Hotoph 3 (or R) test, as it does not record similar results on the same persons.

Lancet, London

1:973-1012 (June 26) 1948

Neuralgic Amyotrophy: Shoulder-Girdle Syndrome. M. J. Parsonage and J. W. A. Turner.—p. 973.
*Vaccination Against Influenza A. Helen Mellanby, J. A. Dudgeon, C. H. Andrews and D. G. Mackay.—p. 978.
Primary Pulmonary Coccidioidomycosis: Case of Laboratory Infection in England. J. D. N. Nabarro.—p. 982.
Postcricoid Pharyngo-Esophageal Perforation Due to Endoscopy Treated by Immediate Suture. J. C. Goligher.—p. 985.
Surgery of Pulmonary Stenosis: Case in Which Pulmonary Valve Was Successfully Divided. T. H. Sellors.—p. 988.

Vaccination Against Influenza A.—Mellanby and her associates state that an attempt was made during the winter of 1946-1947 to test the value of influenza vaccination in Britain. The vaccine used was made from infected allantoic fluids inactivated with 1:2,000 formaldehyde and concentrated by the method of Francis and Salk. Prophylactic vaccination was carried out under controlled conditions during November and December, 1946, in twenty-four mental hospitals, three public schools and numerous small communities, including two preparatory schools, nursing staffs of hospitals and some patients of general practitioners. In eighteen Army training centers alternate intakes were vaccinated. Altogether some 20,000 persons were inoculated, there being about an equal number of uninoculated controls living under similar conditions. In the mental hospitals and in some small groups the incidence of influenza was so low that no conclusions about the efficacy of the vaccine could be drawn. In two out of three schools there were outbreaks of influenza. In one the incidence in the vaccinated boys was 11 per cent and in the controls 21 per cent; in the second the incidence was 11 per cent in the vaccinated and 17.3 per cent in the controls. Outbreaks of disease of the respiratory tract were observed in only three of the eighteen Army units, and one of these the disease probably was not influenzal. In the other two the incidence of influenza was 7.1 per cent in the vaccinated and 8.3 per cent in the controls—not a significant difference. The conclusion is that, in the absence of a widespread epidemic involving many units, a trial on the lines described is unlikely to give a definite answer. The results are much less encouraging than those reported in 1944 and 1946 from the United States. Recent reports from there indicate that in 1947 vaccination had little, if any, effect on the incidence of influenza. Apparently the strains of virus A causing the 1947 epidemics were antigenically rather remote from those contained in the vaccine.

Medical Journal of Australia, Sydney

1:725-752 (June 12) 1948

Other Ways of Doing Things. A. A. Abbie.—p. 725.
Diagnosis of Fallot's Tetralogy and Rationale of Its Surgical Treatment. M. N. Allen.—p. 729.
Surgical Treatment of Fallot's Tetralogy. C. J. Officer Brown.—p. 731.
*Anesthesia in Surgical Treatment of Tetralogy of Fallot. R. H. Orton.—p. 733.
Corneal Transplantations. P. B. English and J. M. White.—p. 736.

Anesthesia in Surgical Treatment of Tetralogy of Fallot.—Orton points out that in the tetralogy of Fallot cyanosis is the outstanding clinical feature. The reasons for its presence, together with its relationship to anoxia, must be considered in order that the physiologic problems that the anesthetist must solve may be understood. At his clinic premedication with morphine was used with the object of lowering the metabolic rate. Atropine was included in the premedication, in spite of its reverse action, owing to the desirability of suppressing secretions in the pharynx. Cyclopropane was administered as the main anesthetic agent, first, as it made possible the use of a high partial pressure of oxygen, and, second, as

controlled respiration is easier with this drug than with ether. Curare was employed as an adjuvant with anesthesia in order to control coughing reflexes and to allow extremely light planes of anesthesia. Control of respiration was established as soon as the larynx had been intubated, and was maintained throughout. In this way adequate pulmonary ventilation was possible in the presence of an open pneumothorax. Further, it was considered that, since the respiratory center in these patients functioned in an abnormal manner, it was preferable to abolish voluntary respiration. Two cases are described in which success was achieved in establishing an artificial communication between the pulmonary and aortic circulations. Since then 9 additional patients with tetralogy of Fallot have been operated on. The method of anesthesia differed in no way from that described.

Proceedings of Royal Society of Medicine, London

41:343-408 (June) 1948. **Partial Index**

Growth and Physical Performance of Children in Relation to Maturity. R. W. B. Ellis.—p. 343.
Surgical Lectures of 150 Years Ago. V. Z. Cope.—p. 353.
Treatment of Congenital Dislocation of Hip. D. Browne.—p. 388.
Hallux Valgus in the Adolescent. A. R. Jones.—p. 392.
Role of Physiotherapy in Treatment of Poliomyelitis. F. S. Cooksey. —p. 395.
Infantile Cerebral Palsy. P. R. Evans.—p. 402.

South African Medical Journal, Cape Town

22:365-388 (June 12) 1948. **Partial Index**

Rings of Labor with Emphasis on Constriction Ring. J. T. Louw. —p. 366.
Health Center Practice in Relation to Private Practice: Memorandum. G. W. Gale—p. 370.
*Soy Bean Culture Medium for Vaccine Production. G. H. Ford and W. Lewin.—p. 372.
*Hiatus Hernia, Diverticula and Gall Stones: Saint's Triad. C. J. B. Muller.—p. 376.

Soya Bean Culture for Vaccine.—Ford and Lewin describe a method for the preparation of a soya bean broth, which was used for the preparation of typhoid vaccine. The vaccine thus prepared was compared with one produced on a meat medium in regard to agglutinin production in rabbits and mouse protection tests and was found not to be inferior to that produced on a meat medium.

Hiatus Hernia, Diverticula and Gallstones.—Muller says that Professor Saint of Cape Town called attention to the association of hiatus hernia, sacculi of the colon and gallstones. Its prognostic importance in avoiding unwarranted treatment, and the differential diagnosis from a host of pulmonary, cardiac and abdominal conditions makes the triad of practical as well as of academic interest. Many references are made in the literature to hiatus hernia and diverticula of the duodenum and colon, hiatus hernia and gallstones, duodenal ulcer and chronic appendicitis, but the author found no reference to the triad of hiatus hernia, diverticula of the colon and gallstones. In the course of making several hundred barium meal studies he observed 3 such cases. The author thinks that more cases of association of this triad of Saint will be found, if they are searched for.

Archivos Argent. Enf. ap. Dig. y Nut., Buenos Aires

22:361-498 (Nov.-Dec.) 1947. **Partial Index**

*Action of Liver Antitoxic Principle in Hepatobiliopathies. J. Nasio. —p. 375.

Action of Liver Antitoxic Principle in Hepatobiliopathies.—Nasio studied the effects of the liver antitoxic principle on a large number of normal persons and on 450 patients with diseases of the liver and of the bile ducts who were observed, in the course of the last five years, at the Argentinean Dispensary for Diseases of the Digestive Apparatus. The liver crystalline substance used by the author was prepared by the American technic. Each cubic centimeter of the substance contains 0.0025 Gm. of the active liver principle as obtained from 50 Gm. of fresh hog's liver. The liver substance was given by intramuscular route in daily dose which varied from 2 cc. to 5 cc., in relation to the more or less acute degree of insufficiency of liver antitoxic principle. The author found that the crystalline antitoxic liver principle is of great value in the therapy of diseases of the liver and the bile ducts. It protects the liver and stimulates elimination through the bile ducts and specific antitoxic function of the liver. The therapeutic effect of the liver antitoxic principle can be evaluated clinically by the Quick test, which is performed before and on the seventh day after administration of a daily dose of 3 cc. of liver antitoxic principle. A good positive response shows by an increased elimination of 50 per cent or more of hippuric and benzoic acids of the Quick test. It indicates a good prognosis and continuation of medical treatment, whereas a negative result indicates either surgical treatment or the presence of an irreversible hepatobiliary disease.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

92:1509-1580 (May 22) 1948. **Partial Index**

Prostatectomy According to Terence Millin. G. L. van der Zwaag. —p. 1517.
*Ascites and Hydrothorax in Presence of Tumors in Lower Abdomen: Syndrome of Meigs. G. Blomhert and Loe Ping Kian.—p. 1523.
*Sporadic Positivity of Sputum. H. C. Hallo and W. C. J. B. Hulscher. —p. 1533.

Ascites and Hydrothorax in Presence of Tumors in Lower Part of Abdomen.—Blomhert and Loe Ping Kian point out that formerly, when accumulations of fluid in abdomen or thorax accompanied a tumor in the genital apparatus, a malignant tumor with metastasis was generally thought of, and only palliative measures were taken as a rule. Meigs and Cass, in 1937, called attention to the fact that a benign tumor may cause ascites and hydrothorax and that such patients can be cured by surgical removal of the tumor. Since then the condition has been known as the syndrome of Meigs. Later studies indicated not only that benign and malignant tumors of the female genital tract may cause this accumulation of fluid in abdomen and thorax, but that this syndrome is an example of a mechanism of much more general occurrence. If certain anatomic and physiologic conditions are fulfilled, any form of ascites, presumably by means of lymphogenous transport, may be accompanied by liquid in both pleural cavities. The authors present a case history which illustrates that tumors of the ovary may be accompanied not only by ascites, but also by hydrothorax.

Sporadically Positive Sputum.—Hallo and Hulscher report that in the course of one year 16 patients were observed in a consultation office for tuberculosis in whom the sputum proved positive during a cold, although clinical and roentgenologic signs indicated that their pulmonary processes were inactive and remained so on further observation. Subsequent cultures of sputum and stomach contents appeared to be negative again. The authors point out that these patients may become the source of infection, although they are regarded as noninfectious.

Semaine des Hôpitaux de Paris

24:1915-1936 (Aug. 6) 1948

*Acute Primary Cardiac Failure in Early Infancy. R. Clément, J. Gerbeaux and R. Nebout.—p. 1915.
Subacute Infectious Dermatomyositis. R. A. Marquézy and J. Bonnette. —p. 1923.

Primary Cardiac Failure in Infancy.—Clément and his co-workers report 4 cases of acute cardiac decompensation in children between the ages of 18 months and 4 years. The clinical picture was identical in all cases. Apparently there was a violent onset of the syndrome. But in reality some accidents of the same type preceded in all cases and were followed by regression. During the first hours disturbances of digestion, particularly vomiting, were of considerable importance. Then the cardiac signs became predominant. There was dyspnea with intense tachypnea and in some instances a galloping rhythm, hepatomegaly and occasionally splenomegaly. The heart volume was enormously increased clinically as well as on roentgenologic examination. Pulmonary stasis was present at the same time. No signs of involvement of the kidneys were observed, and there was complete apyrexia. Complete recovery resulted from treatment with digitalis preparations in 2 patients. The third patient showed considerable improvement, but one year after the initial attack he continued to have attacks of the disease from time to time. The fourth patient was seen by the authors only shortly before death. Necropsy revealed interstitial myocarditis with endocardial thrombosis and mild thickening of the epicardium. The importance of the effect of large daily doses of digitalis preparations is emphasized.

Book Notices

The Biology of Melanomas. By Myron Gordon, and others. Volume IV, Special Publications of the New York Academy of Sciences. Edited by Roy Waldo Miner, Myron Gordon, and Lothar Salin. Being the results of a Conference on The Biology of Normal and Atypical Pigment Cell Growth, held by the Section of Biology of The New York Academy of Sciences November 15 and 16, 1946, New York City. Fabrikoid. Price, $5. Pp. 466, with 107 plates. New York Academy of Sciences, Central Park West at 79th St., New York 24, 1948.

This book is an excellent compilation of material presented at a conference on the "Biology of Normal and Atypical Pigment Cell Growth" held by the section of biology of the New York Academy of Sciences, Nov. 15 and 16, 1946, New York City. Each author, as an active investigator on a phase of pigment cell growth and on development of melanoma, prepared a paper or papers which served as focal points around which the discussions were conducted. These papers have been collected and published as "The Biology of Melanomas."

Thus, all phases of the subject are presented by authorities in their respective fields. The reader is presented first with developmental subjects, followed shortly by a direct introduction to the clinical aspects. Cytologic and genetic studies on the problem are rather well covered, as are the endocrinologic, physiologic and chemical sides. Of particular interest to the clinician are the presentations by Masson, Becker, Pack, MacDonald and Blum. These authors represent a vast total experience, and each has managed to write concisely and thoroughly. The result is a single handbook on melanomas, and for that reason alone is unique among similar textbooks. It should serve as an excellent starting point, or reference work, for beginner and expert alike.

The only criticism is leveled not at the content but the binding. In the text supplied the reviewer, an occasional page was incompletely attached. In general the printing of the text and the illustrations were commendable. Mention is not made of the so-called junction nevus, thought by some investigators at least to be one of the important precursors of the malignant melanoma.

Since the volume contains the points of view of so many different workers on the melanoma problem, it should prove of great interest to all physicians interested in keeping abreast of the times, and especially to those who are responsible for the treatment of benign and malignant melanomas.

Diagnostic Procedures for Virus and Rickettsial Diseases. Thomas Francis, Jr., M.D., Chairman, Committee on Diagnostic Procedures for Virus and Rickettsial Diseases, American Public Health Association. Fabrikoid. Price, $4. Pp. 347, with 20 illustrations. American Public Health Association, 1790 Broadway, New York 19, 1948.

This volume was brought out in recognition of the need for collecting in one source the methodology basic to the laboratory diagnosis of viral and rickettsial diseases. Although designed primarily as a ready reference work for the laboratory worker, it contains much practical information with which the physician should be familiar if he is to keep abreast of the rapid advances being made in this field.

The book represents "a trial flight of a limited nature," and the method of presentation is a part of the experiment. As is pointed out in the preface, there is much repetition as concerns technics; the methods of inoculating embryonated eggs, the technics of the neutralization and the complement fixation tests are described in greater or lesser detail in a number of chapters. While such repetitive description is, for various reasons, perhaps desirable, the apparently myriad modifications of basic methods are confusing to the reader unacquainted with virology. A general chapter on the fundamental technics of egg work, the neutralization and the complement fixation tests would probably have been useful as a background. The inclusion of some discussion of filtration and centrifugation, as used in routine work, and a brief description of tissue culture methods would appear desirable.

Fifteen chapters are devoted to the viral diseases, covering those diseases in which a diagnosis by laboratory methods is possible, if not always feasible. In the latter category is poliomyelitis, whose diagnosis requires monkeys and specially equipped research laboratories—since this is beyond the reach of most institutions, the chapter on poliomyelitis (22 pages) might be considered too long in relation to some others, but actually is a fairly concise, and valuable, summary of current methods. The chapter on yellow fever, comprising 21 pages, is devoted in large part (12 pages) to a detailed description of the neutralization tests for this disease; a condensed version would have served as well and permitted amplification of some of the other methods. On the whole, the various diseases covered are adequately treated from the diagnostic standpoint.

In any routine diagnostic laboratory, certain practical considerations are highly important in its operation, and these, while not necessarily treated academically, have not always been given their proper perspective. For example, isolation of viral or rickettsial agents is primarily a concomitant of investigative work; from the standpoint of a laboratory concerned primarily with diagnosis, isolation of an agent is warranted only under special circumstances, since its recovery seldom provides information which cannot be obtained more simply and with less expense by serologic methods. Similarly, the dictum that serum after collection should immediately be frozen on solid carbon dioxide and sent to the laboratory packed in this refrigerant is susceptible of fulfilment only by those research laboratories which collect their own field material; a laboratory dealing with hundreds or thousands of physicians for obvious reasons finds such a procedure impractical of achievement. Storage of serums at below freezing temperatures is also a factor in any laboratory with a large diagnostic load.

The rickettsial diseases are covered in two chapters comprising a total of 34 pages. One chapter deals with the isolation and identification of the rickettsial agents; the other with serologic procedures for the diagnosis of rickettsial diseases. The treatment is clear and succinct, and the two chapters, while brief, are an excellent collation of material widely scattered in the literature of this group of diseases.

Comparative Physiology. By Bradley T. Scheer, Ph.D., Assistant Professor of Biochemistry, University of Southern California, Los Angeles. Cloth. Price, $6. Pp. 563, with 72 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, 1948.

This new book, written as a textbook for an advanced university course in comparative physiology, will interest the student of mammalian physiology, collecting, as it does, the scattered literature on the physiology of the so-called lower animals.

After an opening chapter on the biochemical and physiologic processes generally thought to be common to all animals, the author surveys the animal kingdom from protozoa through vertebrates, taking up, in turn, the protozoa, the multicellular acelomate animals (the sponges, coelenterates, flatworms and roundworms), the Mollusca and the Annelida. There follow two chapters on the Arthropoda—the first dealing with the Crustacea in general and Limulus, the horse shoe crab in particular, and the second dealing with the insects. One chapter is devoted to the Echinodermata and two to the Vertebrata.

Within each chapter the physiology of each of these groups of animals is taken up under such headings as nutrition, feeding, digestion, circulation, respiration, metabolism, excretion, regulation of the internal environment, neuromuscular systems, central nervous systems, locomotions, sense organs and behavior.

At the end of each chapter, and in a final concluding chapter, there are summaries in which the salient features of each phylum are discussed. Particular attention is paid to the important ecologic and evolutionary developments within each phylum.

This arrangement of material enables the author to summarize the existing information and thus present a uniform picture of the physiology of each animal type. It points up the utility of particular physiologic adjustments in terms of the ecologic environment and of the behavior of the animal. Finally, it enables the author to interpret, by comparative methods, the physiologic as well as the morphologic changes which have occurred during the course of evolution.

Much of the latter interpretation is put forth frankly as hypothesis, in the hope that further experimental work will be

stimulated. It is clear from a reading of the book that such further work is vitally needed. Virtually no information of a physiologic nature is available about many animal types. Thus, although ten different phyla are discussed, almost a third of the book is devoted to one class, the Vertebrata.

There is an appendix giving a broad classification of animals, a species index and a subject index. Although there are over eight hundred references, there is no author index.

Hipófisis y crecimiento (estudio experimental). Por Héctor E. J. Houssay. Paper. Pp. 293, with 68 illustrations. El Ateneo. Córdoba 2099, Buenos Aires, 1947.

This is an interesting and valuable monograph from the pen of the son of Dr. Bernardo Houssay, who is so well known to the world of science. He was helped by his mother, also a physician. He first reviews the effects of hypophysectomy on the growth of animals, mainly puppies. The failures in growth seem to be due particularly to an insufficiency of function in the pars distalis. The defective growth was not modified by the daily ingestion of fresh beef hypophysis, but it was corrected by the injection of extracts of the anterior hypophysis. Houssay described the appearance of the puppies which failed to grow. He studied the defective calcification of their bones. Much of the failure to grow shows in the cartilage. There is a tendency to retain the first temporary teeth. There is a tendency also to adiposity. Sometimes there is infiltration of fat into the liver. The skin may be thick and infiltrated. The hair remains infantile. There may be some failure of development of erythrocytes and hemoglobin. There are, of course, marked alterations in the development of the endocrine glands. The thyroid gland is small, pale and undeveloped. The ovaries and testicles are small. Parts of the adrenals are atrophic. The basal metabolic rate is low. The metabolism of protein is deficient, and this has much to do with the failure in growth. The excretion of nitrogen, creatinine and phosphates is low. There are decided changes in the metabolism of carbohydrates. The blood sugar falls rapidly during fasting, and the animals are highly sensitive to insulin or phlorizin. Occasionally there is transient polyuria. The blood calcium is normal. The serum potassium tends to be low. The animals tend to be apathetic, slow, timid and foolish. They are abnormally sensitive to infection. Often they lose their appetite.

There is a chapter on the effects of hypophysial disease in man, and there is a large bibliography.

The Digestive Tract in Roentgenology. By Jacob Buckstein, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College, New York. Fabrikoid. Price, $16. Pp. 889, with 1030 illustrations. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

This revised edition of a well known textbook presents many additional roentgenographic data on the gastrointestinal tract and associated structures. The book is well written and contains many studies of extreme interest to the radiologist and gastroenterologist. Each section contains a brief review of the normal roentgenologic anatomy as well as roentgenographic technic. Case histories accompany the illustrations, giving pertinent clinical differential points in a brief but adequate summary.

The reproductions of the roentgenograms have been done unusually well and are very clear. Many photographs of specimens are included to complete the case studies and to permit a more thorough correlation of the pathology and the roentgenographic appearance. The reproductions demonstrate the roentgenographic appearance of many phases of both the common and the unusual disease conditions of the gastrointestinal tract.

The roentgenograms illustrate almost all the lesions encountered in the alimentary tract in the adult. The author, however, has neglected to include a study of the postoperative appearance of the colon and esophagus, which may be an extremely difficult problem to evaluate from a roentgenographic standpoint. The studies of the gastrointestinal tract of the infant include the more common lesions encountered, but they are covered in a rather sketchy fashion. Many of the problems encountered in the study of the gastrointestinal tract of the infant and child are omitted completely.

The section on cholangiography again emphasizes the value of the procedure along with valuable notes on the proper technic. The small intestinal lesions are thoroughly covered. The studies presented are adequate, but improvement could be accomplished by the reproduction of spot film roentgenograms for study of the changes noted at the fluoroscopic examination.

Most of the diagnostic procedures are covered well, and the author does an excellent job of covering the multitude of pathologic changes encountered in the gastrointestinal tract. The material is presented in a clear and concise manner which makes for easy reading.

Gardiner's Handbook of Skin Disease. Revised by John Kinnear, O.B.E., T.D., M.D., Physician for Diseases of the Skin, Dundee Royal Infirmary, Dundee. Fifth edition. Cloth. Price, $4.50. Pp. 250, with 100 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

The reader will find this book interesting but not of great practical value. The interest lies in the author's descriptive writing and in his broad concept of dermatology, both of which will appeal to the practitioner rather than to the undergraduate student. As in most handbooks which try to cover a vast field in small space, the descriptions and discussions are much too brief and there are no references to pertinent literature. Emphasis is placed on the common dermatoses, and many of the newer developments in dermatology have been included in this edition, but the author's methods of treatment differ somewhat from those practiced in this country. The book does have the virtue of being a personal work in every sense, reflecting the author's views and experience both in civilian and military practice. As such, it should be a worth while addition to any one's dermatologic library.

The Clinical Picture of Thyrotoxicosis. By Peter McEwan, M.A., M.B., Ch.B. Cloth. Price, 15s. Pp. 127, with illustrations. Oliver & Boyd, Ltd., Tweeddale Court, 14 High St., Edinburgh 1, 1948.

This small volume represents the effort of a Yorkshire surgeon to portray the clinical picture of thyrotoxicosis from a "practical" point of view. It is highly personalized, and is based on the author's experience with about two thousand thyroidectomies over a period of twenty-five years. It contains twenty-five sections dealing with such aspects of thyrotoxicosis as the classical signs and symptoms, the cardiac state, the basal metabolic rate, ocular phenomena, thyrotoxicosis and pregnancy, the thyrotoxic crisis, differential diagnostic problems, and general considerations of surgical treatment and the use of thiouracil and related compounds. The twenty-fourth section is devoted to an attempt to analyze and interpret the mortality statistics for thyroid disease from the office of the Registrar-General for England and Wales from 1913 through 1945.

Unfortunately this effort possesses many faults and few virtues. The author's treatment of his subject is based almost entirely on personal impressions which are submitted with practically no statistical data for support. There is no discussion of pathology or pathologic physiology, and the bibliography is scant, with little reference to the important advances in thyroid disease made by American investigators. The author's case reports are so sketchily presented and poorly documented that no critical evaluation of them is possible. Some of his statements are remarkable, and certain controversial points are treated dogmatically; thus, he recommends thyroidectomy for all pregnant thyrotoxic patients, and gives quinidine a blanket endorsement in the treatment of postoperative thyrotoxic auricular fibrillation. He has entirely abandoned the use of basal metabolism determination in diagnosis. He condemns the use of iodine for differential diagnosis. He states that he has never seen coexistent thyrotoxicosis and active pulmonary tuberculosis. On page 28 he states, "The irregular pulse carries with it, in my experience, no special risk"; on page 117, "It is justifiable to infer that auricular fibrillation is a serious complication of thyrotoxicosis."

There is no discussion of the management or of the differential diagnosis of thyrotoxic heart failure, and no consideration of diabetes, avitaminosis or hepatic damage in thyrotoxicosis.

An unjustifiable attempt is made to create specific symptom patterns for certain occasional complaints or manifestations which are by no means characteristic of thyrotoxicosis. Thus,

there are descriptions of the typical headache, the voice changes, abdominal, extremity and back pains, and urinary symptoms which are alleged to be frequent components of a specific thyrotoxic symptom complex. With due allowance for geographic variations in the thyrotoxic syndrome as it exists in England and the United States, it will be difficult to agree with many of the author's impressions and conclusions, and his book cannot be considered as an important contribution to the literature of thyroid disease.

The Sulphonamides and Allied Compounds. By Elmore H. Northey, Ph.D., Administrative Director, Stamford Research Laboratories, American Cyanamid Company, Stamford, Conn. American Chemical Society Monograph Series. Cloth. Price, $12.50. Pp. 660, with 8 illustrations. Reinhold Pub. Corp., 330 W. 42nd St., New York 18, 1948.

The information contained in the monograph makes available to the medical profession an accurate digest of the work done in a large and important chemotherapeutic field. It also permits a proper evaluation of that work and points out certain areas in which additional research may be profitable.

The monograph gives a fairly complete survey of the experimental work in the field of sulfonamides and related compounds. The book is divided into twelve chapters, seven of which are devoted to the chemistry and pharmacology of simple and complex sulfanilamide derivatives and of sulfones and related compounds. Most of the sulfonamides and sulfones which have been prepared and tested are arranged in convenient tables which list their activities with respect to various organisms and give appropriate references. The compiled material is grouped into 323 tables and contains 2668 references.

The volume also includes chapters on the experimental method used in the evaluation of chemotherapeutic activity, the relationship of structure to activity, theories concerning the mechanism of the action of sulfonamides and sulfones and a clinical evaluation of the sulfonamide drugs.

Foundations of Neuropsychiatry. By Stanley Cobb, A.B., M.D., Bullard Professor of Neuropathology, Harvard Medical School, Boston. Fourth edition of the work formerly known as A Preface to Nervous Disease. Cloth. Price, $2.50. Pp. 260, with 13 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

Any book that reaches a fourth edition must be able to satisfy a need in American medicine. That certainly is true of Dr. Cobb's, "Foundations of Neuropsychiatry." In simple language he covers the basic fundamentals that a student of the nervous system needs to know. If there is any criticism, it is that not enough of the psychologic foundations of psychiatry itself are included. However, for the audience toward which this book is directed it is exceedingly satisfactory.

Practical Bacteriology, Hematology, and Parasitology. By E. R. Stitt, M.D., Ph.M., Sc.D., Paul W. Clough, M.D., Physician-in-Charge of the Diagnostic Clinic, Johns Hopkins Hospital, Baltimore, Sara E. Branham, M.D., Ph.D., Sc.D., Senior Bacteriologist, National Institute of Health, and others. Tenth edition. Fabrikoid. Price, $10. Pp. 991, with 765 illustrations. The Blakiston Co., 1012 Walnut St., Philadelphia 5; Toronto 2, 1948.

Fortunately, the original author is still living to enjoy the popularity of this book, although it first appeared some forty years ago. Each of the many editions has given more space to the interpretation and diagnostic significance of laboratory procedures. The various sections of the book have been revised, and some sections have been entirely rewritten. The chapter on examination of the cerebrospinal fluid has been extensively revised, and a new method of preparing colloidal gold solution now in use in the Naval Medical School laboratories is included. Dr. Reuben Kahn has reviewed the section dealing with the Kahn flocculation test. Dr. John Kolmer reviewed the technic of the Kolmer complement fixation test. The chapter on filtrable viruses has been rewritten by Dr. Paul W. Clough and new material added, particularly on poliomyelitis, influenza, infectious hepatitis, the encephalitides and primary atypical pneumonia. The section on rickettsial diseases was written by Dr. Norman H. Topping and includes descriptions of Q fever and scrub typhus. Some material in the previous edition has been omitted from this one to make room for recent advances in this field. In this way, it has been possible to keep the size of the book about the same.

Dermatologic Therapy in General Practice. By Marion B. Sulzberger, M.D., Professor of Clinical Dermatology and Syphilology and Director, Department of Dematology and Syphilology, New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, New York, and Jack Wolf, M.D., Attending Dermatologist and Syphilologist and Chief of Service, New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Third edition. Cloth. Price, $7.75. Pp. 663, with 66 illustrations. Year Book Publishers, Inc., 304 S. Dearborn St., Chicago 4, 1948.

This third edition brings up to date the important advances in dermatologic and antisyphilitic therapy. It is written primarily for the general practitioner and contains information which, if wisely used, will enable him adequately to treat most of the common dermatoses. In a logical and straightforward manner the principles of therapy are discussed. Thus, before specific measures are mentioned. the first chapters are devoted to general principles of topical medication and physical therapy. The authors make an excellent attempt to enable the reader to understand the reasons for using each type of local medication so that it may be applied with an intelligent understanding for the needs of dermatologic patients. Whole chapters are devoted to the diagnosis and treatment of such disorders as: the eczematous dermatoses, urticaria, atopic eczema, fungus diseases, acne vulgaris, the pyodermas, seborrheic dermatitis, parasitic diseases and new growths. The chapters on syphilis deal with the clinical features of the disease as well as newer methods of treatment. This book is not one for reference only but for the daily use of all who feel the need to be better informed about the management of dermatologic patients.

Industrial Psychology. By John Tiffin, Ph.D., Professor of Industrial Psychology, Purdue University, Lafayette, Indiana. Second edition. Cloth. Price, $5.35. Pp. 553, with 140 illustrations. Prentice-Hall, Inc., 70 Fifth Ave., New York 11, 1947.

One of the major functions of the physician in industry is to match the requirements of jobs with the physical, mental and emotional abilities of employees. Industrial psychology deals essentially with the temperamental adaptations and aptitudes of persons for jobs. Tiffin's current revision is an excellent compilation of present uses of psychology in employment procedure and in the larger problems of industrial human relations. Every chapter contains much new material. The physician in industry will profit by his discussions of the technics of interviewing, employee testing, job analysis and evaluation, training methods and of the factors governing efficiency, productive work, safety and morale.

Manual técnico de hemoterapia para médicos generales y estudiantes. Por el Dr. Augusto M. Romero Alvarez, jefe del banco de sangre regional del oeste (Instituto de cirugía de la Provincia de Buenos Aires, Haedo, F. C. O.). Paper. Pp. 103, with 23 illustrations. Productos Roche S. A., Buenos Aires, [1948].

This is a handy booklet, well illustrated and of practical value for all physicians who from time to time want to give transfusions. The author states that the first physician to give a transfusion of citrated blood was Dr. Luis Agote of Buenos Aires. This was given on Nov. 9, 1914. The first man to show that one should transfuse only human blood into man was Dr. Blundell. He wrote in 1828. This is a handy little book of 103 pages and, if translated, might well be popular in this country.

Hawaii Diet Manual, Hawaii Dietetic Association. Compiled by Diet Therapy Committee. Boards. Loose-leaf. Price, $5. Pp. 192. Hawaii Dietetic Association, Honolulu, 1947.

This book is a guide for diet therapy in the territory of Hawaii with modifications of standard procedure suited to the locality. Also listed are diets peculiar to national groups found in Hawaii. This enables the therapist to prescribe an effective diet with due consideration for the patient's customs and food preferences. This work will undoubtedly find wide use in Hawaii by the physicians, dietitians, nurses and other interested professional groups working there.

Pediatrics for Nurses. By Arthur G. Watkins, M.D., F.R.C.P., Physician in Children's Diseases, Cardiff Royal Infirmary, Cardiff. Cloth. Price, $3.50. Pp. 192, with 22 illustrations. Williams & Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2, 1948.

This is an excellent small monograph of pediatrics. The material is well organized and presented in an interesting manner. Schools of nursing will find it a good text to use.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

INDICATIONS FOR DIGITALIS

To the Editor:—**Is digitalis (any form) indicated or advisable in the following conditions: (1) paroxysmal auricular tachycardia (to avoid future attacks); (2) when electrocardiograph evidence is present of strain of the left and/or the right side of the heart with hypertension (diastolic) but with no definite clinical evidence of failure other than dyspnea; (3) when systolic pressure is high, diastolic is normal, with respiratory distress and numerous dry rales of the chest but with normal circulation time? There is no other evidence of failure.**

Anthony M. Susinno, M.D., Palisades Park, N. J.

ANSWER.—In simple auricular or atrioventricular paroxysmal tachycardia in which attacks occur frequently (once per week or more often, for example) digitalization by any method sometimes greatly reduces the frequency of the seizures. There is no objection to its use for this purpose if it is effective and if the repeated attacks make the patient particularly uncomfortable. In paroxysmal auricular fibrillation or flutter in which the attacks are frequent, digitalization may not reduce the number of the attacks but it usually conspicuously reduces the ventricular rate during them and thus reduces or prevents the symptoms which they produce. Quinidine may also be tried in any of these circumstances; it is particularly effective in paroxysmal ventricular tachycardia, in which the administration of digitalis is usually inadvisable.

No type of change in the form of the electrocardiogram can be regarded under any circumstances as an indication for the administration of digitalis. The electrocardiographic changes referred to as indicative of strain of right or left side of the heart are not, by themselves, a reason for giving this drug, regardless of the level of the blood pressure. Dyspnea, when there are strong reasons for believing that it is of cardiac origin, is an indication for giving digitalis. In most cases, however, dyspnea which is brought about by cardiac weakness increases rather rapidly in severity. The complaint of shortness of breath is so common and arises in so many different ways that it should be ascribed to beginning heart failure only after careful investigation.

Respiratory distress with dry rales is more often due to infection of the respiratory tract or bronchial spasm than to cardiac failure alone. In some patients with pulmonary congestion of cardiac origin a kind of asthmatic bronchitis develops which is rather persistent and tends to clear up as the cardiac condition improves. This clinical syndrome is much less serious than respiratory distress with distinctly moist rales, but it may be helped by the administration of digitalis and aminophylline. Epinephrine may give relief but should not ordinarily be used in cases of the kind referred to.

ERYTHROBLASTOSIS

To the Editor:—**I have a 29 year old white patient, who had one pregnancy three years ago; a normal full term male infant was delivered uneventfully. She is Rh negative and her husband is Rh positive. She is now two and one-half months pregnant. History of an abortion is absent. What course should be pursued in caring for her?**

M.D., Tennessee.

ANSWER.—The pregnant woman should be tested immediately for Rh antibodies. If the result of the test is negative, it should be repeated at frequent intervals throughout the pregnancy. There is a relation between the time of appearance of Rh antibodies in pregnancy and the severity of disease in the fetus and infant. The height of the titer has a similar significance. On the other hand, finding of antibodies during the first trimester suggests strongly that they are due to the immunizing action of a preceding pregnancy. In such case the interpretation is made more difficult. A history of a previous transfusion of Rh-positive blood makes the prognosis worse.

The parents of the husband and the first child should be tested, and if any of them is found Rh negative, heterozygosity of the husband is established. That offers a good chance (up to 50 per cent) of an Rh-negative infant, not subject to fetal erythroblastosis due to Rh incompatibility. Heterozygosity of the husband is not excluded even if his parents are Rh positive. If the husband is Rh_1 (CDe), testing his blood with the rare anti-hr′ (anti-c) serum may be another means of establishing heterozygosity. He is heterozygous Rh positive if he is hr′ positive. He is homozygous Rh positive if he is hr′ negative and all his children will be Rh positive and more likely to be affected by erythroblastosis. If antibody tests during pregnancy suggest the possibility of disease in the fetus, Rh-negative blood of suitable blood group should be made available at the time of delivery to permit prompt transfusion if signs of disease are present.

The mother does not require any special care, because her well-being is not affected by the process of Rh sensitization. If she were in need of a transfusion, only Rh-negative blood must be used.

The answer to the question regarding the mother's chances of successful termination of this pregnancy depends partly on the circumstances discussed previously. On the basis of available statistical data in the absence of a previous history of erythroblastotic children the chances are about 96 in a hundred that the child will not be affected.

BISMUTH SALICYLATE

To the Editor:—**What information can you give me as to the toxic effects of prolonged intramuscular injection of salicylate in oil, at a dosage of 2 cc. per week? How long may such a dose safely be given? Are there any references regarding this medication in the treatment of psoriasis?**

M.D., New York.

ANSWER.—Presumably from the fact that it is administered intramuscularly and in oil, the query refers to bismuth salicylate. The usual practice is to administer insoluble bismuth in courses of ten to fifteen weekly injections, followed by a rest period of one month. Some physicians administer it regularly without rest periods for a year or longer, provided, of course, that there is no evidence of harm from its use. Whenever bismuth is used, the urine should be examined at frequent intervals for evidence of renal damage and the gums and tongue should be examined for evidence of blue lines. Like other heavy metals, the drug may also produce toxic reactions in skin, liver, nervous system and hemopoietic system and such local reactions as abscess formation or arterial emboli. Bismuth compound, like numerous other preparations, has been used for the treatment of psoriasis, but has no special virtue.

SULFUR DIOXIDE POISONING

To the Editor:—**Please furnish information on sulfur dioxide inhalation and poisoning. What are the lethal dose, toxicity and symptoms caused by inhalation, complications and disability?**

M. J. Stec, M.D., Scranton, Pa.

ANSWER.—Sulfur dioxide is one of the more active irritant gasses and probably produces greater pain than almost any other industrial gas. Irritation begins at about the level of 10 parts per million. Exposure at any higher level over long periods will lead to physiologic response. At and above 500 parts per million even short exposures are dangerous. On its reaching mucous membranes the moisture there present combines with the sulfur dioxide, suggesting that the ultimate action is that of the sulfur acids. In gross concentrations, spasm of the laryngeal area somewhat effectively bars off the entry of the gas and gives rise to the term "irrespirable." It thus comes about that the tissues of the upper respiratory tract may be more involved than the lungs themselves. From lower and commoner concentrations, there may promptly arise inflammation of all membranes, violent coughing and sneezing, pharyngitis, laryngitis, bronchitis or pneumonitis with or without pulmonary edema. Bronchial pneumonia may arise. Among those long exposed there may appear digestive disturbances, impaired senses of smell and taste, excessive urinary acidity, increased fatigability and dyspnea. Action is not limited to the respiratory tract and may involve the eyes. The skin is little damaged, but sulfur dioxide in water may provoke dermatitis; a chronic state has been described resembling furunculosis. The action of sulfur dioxide is not persistent, so that a true chronic state does not arise except that chronic exposure perpetuates acute manifestations. After cessation of exposure all manifestations tend to disappear. However, on rare occasions it is possibly true that a condition of allergy, or akin to allergy, develops to the end that subsequent trivial exposures excite responses out of proportion to those expectable.

In the use of sulfur dioxide as a liquid, as in refrigeration, minor leaks may lead to sulfur dioxide spurts, with rapid and painful freezing of eyeballs. Contrary to some common belief, sulfur dioxide involvement of the lung does not predispose to, or accelerate, tuberculosis. Workers using this gas apparently acquire a fair degree of tolerance. Actually a lack of response may result merely from the coating of the respiratory passages by a layer of tenacious secretion.

SUBACUTE COLITIS

To the Editor:—A white woman, aged 38, has been suffering from diarrhea, epigastric pain and low grade fever for the past five months. There are six to ten stools almost every day. (Only occasionally are there one to two stools in twenty-four hours.) Sometimes the stools are normal in shape and appearance: often there is mucus, and some stools appear purulent. These, microscopically, are practically pure pus, mostly polymorphonuclear leukocytes. Very rarely is there occult blood. The epigastric pain occurs almost daily, sometimes radiating to one or both shoulders. Often the pain is apparently entirely thoracic. The pain is always colicky and may last for several hours. The temperature ranges from 99 to 101 F. Proctoscopic examination on two occasions did not reveal any abnormality, nor did barium enema. Barium compound orally showed irritability of the bulb of duodenum. Standard therapy for peptic ulcer has had no effect on symptoms. Examinations of stool did not show parasites or amebas. The white blood cell count is 12,000, and the sedimentation rate varies from 25 to 40 in one hour. Antispasmodics (belladonna, papaverine) and usual gastric "sedative powders" have been ineffectual. A series of eight colonic irrigations had been undergone and to the naked eye produced much mucus, pus and, on two occasions, what the therapist called "gravel." A consultant made the diagnosis of "irritable bowel" and recommended the antispasmodics and colonic irrigations, as mentioned. While this diagnosis seemed untenable in view of the fever and purulent stools, his advice was carried out, with no effect on symptoms. A cholecystectomy was done four years ago (because of gallstones) and the health has been excellent until the present illness. The history strongly suggested ulcerative colitis to me, but this cannot be demonstrated proctoscopically or roentgenologically. What further studies are indicated? Is the use of penicillin or the sulfonamide compounds indicated on an empiric basis? If so, which is preferable? If penicillin is advised, what dosage is recommended?

M.D., New York.

ANSWER.—The accurate diagnosis of chronic diarrhea, fever and abdominal pain occasionally is very difficult and accomplished only after prolonged observation and study. Since regional enteritis may cause colicky abdominal pain, diarrhea, fever, leukocytosis, an increased sedimentation rate and blood in the feces, further effort should be made to visualize the small bowel by barium enema and by serial roentgenograms after the oral ingestion of barium compound. Additional information regarding the physical findings, including the pelvic and rectal examinations, would be helpful. A mass in the lower part of the abdomen or high in the pelvis, for example, would support the diagnosis of regional enteritis. Repeated cultures should be made of the feces for pathogenic bacteria, including Salmonella and dysentery organisms, to exclude some type of enteric infection. Cultures of the blood and urine and the various serum agglutination reactions are indicated in view of the unexplained fever. Subphrenic, hepatic or perinephric abscess might be considered, as well as a pelvic abscess discharging into the rectum. The radiation of pain to the shoulders suggests diaphragmatic irritation. Tumors of the gastrointestinal tract or neoplasms arising in the pelvis and involving the bowel sometimes manifest themselves primarily by fever. The various diagnostic procedures should be repeated, especially the roentgen examinations of the small intestine and colon and the proctoscopic examination at intervals. The most likely diagnosis with the evidence offered is regional enteritis or colitis.

Management, in the absence of a specific etiologic factor, is symptomatic. The use of a bland, low residue, nonlaxative diet is indicated. Antispasmodics and sedatives, such as phenobarbital, ¼ to ½ grain (15 to 30 mg.), and extract of belladonna, ⅛ grain (8 mg.), four times daily may be helpful. Colonic irrigations are not indicated. Sulfonamide compounds and penicillin should be withheld until a specific indication arises. More definitive therapy depends on more precise diagnosis.

COCCIDIOIDOMYCOSIS

To the Editor:—Is there any specific treatment for coccidioidomycosis? Is serum for the coccidioidin skin test available?

Erich Seligmann, M.D., Whitehall, N. Y.

ANSWER.—1. Specific treatment for coccidioidomycosis is lacking. The object of treatment in the primary and disseminated forms is to assist the patient in focalizing his lesions. This is best accomplished by bed rest, adequate diet and symptomatic treatment during the stage of activity of the disease. Activity is indicated by fever, elevated erythrocyte sedimentation rate, rising titer of complement-fixing antibodies and progression or instability of the pulmonary lesions as determined by serial roentgenograms. All drugs used thus far, including the sulfonamide compounds, penicillin and streptomycin, have been ineffective. Vaccine treatment as recommended by Jacobson and immunotransfusion have not been generally accepted as influencing the course of the disease. Of the benign pulmonary residues, such as nodules and cavitation, only the latter may rarely require treatment and then only for severe or recurrent hemoptysis. Pneumothorax, phrenicolysis and immobilization of the thorax with weighted bags have been used. Such measures are difficult to evaluate because of the natural tendency to spontaneous healing, even after long periods. It is doubtful whether more radical procedures, such as used in the treatment of tuberculous cavitation, are ever justifiable.

2. Material for the coccidioidin skin test is not available commercially. Technical difficulties in production and a restricted market have delayed or prevented pharmaceutic houses from producing coccidioidin commercially. Teaching institutions or Veterans' Administration hospitals may have available a small supply of coccidioidin.

SPEECH DELAY

To the Editor:—I have a patient, 7½ years old, who cannot talk. The boy is able to make sounds and can laugh. Occasionally he will say a word. His parents have taken him to Children's Hospital and to a speech specialist in Boston. The answer received is that there is nothing that can be done, but that the boy will speak in time. I have not found any abnormal condition. Is there any way in which this boy can be tested to find out whether he will ever speak? Please suggest a method of handling this boy.

Robert H. Goldman, M.D., Leominster, Mass.

ANSWER.—Delayed speech may be due to mental retardation or it may be due to lack of hearing to such a degree that the child cannot learn speech or it may be due to neither of these causes, in which case it is described as motor speech delay or delay in learning to speak. Children of 7 sometimes do not speak, though later they learn to speak clearly. There are clinics in Boston in which these conditions are recognized, and adequate treatment is planned wherever possible. One of these clinics is at the Children's Hospital; another is the Language Clinic at the Massachusetts General Hospital. Either of these clinics could give the doctor and the family involved good advice. The condition is often baffling.

HISTOPLASMOSIS

To the Editor:—I examined a white woman aged 35 years and her daughter aged 6. In 1943 histoplasmosis organisms were found in large quantities in the spinal fluid of the child and in the blood of the mother. An encephalogram showed dilatation of the lateral and third ventricles of the child. The mother was advised to have no more children and underwent a sterilization operation. In the child an amentia with athetoid quadriplegia has developed. The mother has remained in good health for the past five years. There have been no clinical efforts to determine the presence or absence of the infection in mother or child since 1943. Your opinion is requested as to the advisability of the mother's submission to any type of clinical test for the presence or absence of her infection. If she still carries the fungus, is there any effective treatment?

M.D., Mississippi.

ANSWER.—Infection with Histoplasma capsulatum has been observed only once before to give rise to clinical disease in members of the same family. McLeod and associates reported its occurrence in siblings (*J. Pediat.* **28**:275, 1946). The apparent simultaneous involvement of a mother and her child is, therefore, unique so far as is known. Knowledge of the epidemiology of histoplasmosis is incomplete, and it is suggested that details of these cases be reported for their possible bearing on this aspect of the problem.

It would be most important to establish whether or not these patients still harbor the organism. H. capsulatum may be isolated by various cultural methods (Parsons, R. J., and Zarafonetis, C. J. D.: *Arch. Int. Med.* **75**:1 [Jan.] 1945). Sources of inoculum include the blood, bone marrow, spinal fluid, sputum and biopsy material from lymph nodes or superficial ulcerations. Blood agar slants (incubated at 37.5 C.) and Sabouraud's mediums (incubated at room temperature) are commonly used for cultivation of the organism. Yeastlike growth occurs on the former, while the latter yields the characteristic mycelial phase.

Microscopic examination of sections of biopsy material may reveal encepsulated intracellular organisms. Their presence cannot be considered diagnostic, however, since there are other organisms which at times are morphologically indistinguishable from H. capsulatum in tissue sections. The diagnosis of histoplasmosis can, therefore, be established with certainty only by strain isolation.

Additional diagnostic aid may be forthcoming from serologic tests for histoplasmosis. Complement fixation (Salvin, S. B.: *Proc. Soc. Exper. Biol. & Med.* **66**:342, 1947) and precipitin (Pates, A. L.: *Science*, to be published) reactions have been obtained in tests on serums from patients and animals infected with the causative agent. These tests are, however, still in the experimental phase.

Cutaneous tests with histoplasmin antigens will contribute nothing toward establishing the presence or absence of active

infection in these patients. A brief discussion of the diagnostic value of histoplasmin cutaneous tests may be found in this department of THE JOURNAL, Oct. 25, 1947, page 543. In the same reference are listed the various therapeutic agents which have been tried, generally without success, in the treatment of histoplasmosis. In addition, J. H. Seabury (unpublished work) has used "promin" (sodium p,-p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) in the treatment of 2 patients with histoplasmosis. "Promin" therapy has also been undertaken in experimentally infected dogs. Preliminary results appear encouraging, and further studies are under way. Details of the "promin" treatment schedules employed by Dr. Seabury may be obtained by an inquiry addressed to him at the Louisiana State University School of Medicine, New Orleans.

NEUROSIS

To the Editor:—A white man aged 28 years had complained for many years of a peculiar skin sensation which he is unable to describe exactly. The nature of his complaint—which is not a real pruritus, though he uses the word "itching" occasionally—is best described as the patient's being "skin conscious." His skin is at times so sensitive that he becomes irritated when anybody, even his young wife or baby, touches him. He feels best with all clothing removed. Neurologically he was found to be normal. Tests of spinal fluid and blood serum were negative in result. Clinical studies showed at some time the following abnormalities: (1) prostatitis, chronic, which responded to treatment and did not recur; (2) moderately irritable colon; (3) allergy to mushroom, peas, currants, raisins, blackberries, cinnamon, thyme and hops; (4) moderate hyperacidity with loose bowel movements and occasional diarrhea; a complete blood cell count (eighteen months previously) showed 90 per cent hemoglobin and 3,900,000 red blood cells without poikylocytosis and anisocytosis. After several months of liver therapy, the blood was normal; the condition of the skin remained the same. Other treatment consisted of foreign protein, auto hemotherapy, diets, large doses of vitamins A and B, vitamin B complex, ultraviolet radiation, "bellergal" (a proprietary compound of belladona alkaloids, ergotamine tartrate and phenobarbital), "belladenal" (a mixture of belladonna alkaloids and phenobarbital), calcium gluconate, sodium nicotinate, galvanic baths, anti-histaminics and histamine desensitization. A psychiatrist diagnosed conversion syndrome (guilt complex—a brother was killed by gas). The patient termed the treatment unsuccessful and stopped the sessions with the psychiatrist after five sessions. Do you believe this to be a psychosomatic case? If not, what other diagnosis and treatment should be considered?

M.D., New York.

ANSWER.—It would seem that this patient's complaints are entirely psychosomatic in nature. All investigations have failed to establish an organic cause and the usual treatment measures have been used to no avail. Since a diagnosis of conversion syndrome has been made in his case, he should be encouraged to cooperate with his psychiatrist in an attempt to solve the problem.

CIGARET HABIT

To the Editor:—A patient is desirous of discontinuing smoking of cigarets. He is of a nervous disposition and thinks that it would be an easier task if some medical aid could be given to him. How can I be of help to this man?

M.D., Indiana.

ANSWER.—The patient who wishes to discontinue the smoking of cigarets may secure instruction and support from reading accounts of successful ex-smokers (Furnas, J. C.: So You're Going to Stop Smoking, New York, Simon & Schuster, 1938). Rinsing the mouth or swabbing the throat with 0.5 per cent silver nitrate, causing distaste on smoking, has been used. Acute symptoms of deprivation or nicotine withdrawal, with tremors and nervousness, suffered by some smokers immediately on cessation of smoking may be lessened by taking candy or otherwise raising the blood sugar and compensating for the lack of habitual adrenal stimulation from nicotine (Cannon, W. B., and others: A Note on the Effect of Nicotine Injection on Adrenal Secretion, *J. Pharmacol. & Exper. Therap.* **3**:379, 1911). The conditioned reflex, or habitual handling of cigarets, may be bridged by chewing gum.

SUSPENSORIES

To the Editor:—What deleterious effects result from continued use of a supporter or a suspensory on testicular function, (*a*) general and (*b*) spermatogenic?

M.D., Pennsylvania.

ANSWER.—Continued use of a supporter or a suspensory should not have deleterious effects on testicular function, either general or spermatogenic. The only exception to this statement would be in an unusual instance in which the use of such a support would cause constriction of the spermatic cord with interference of the normal blood supply of the testes. Such a condition would be intolerable to the patient, and the supporter would be discarded.

PLASTIC REPAIR OF FALLOPIAN TUBES

To the Editor:—A patient, 30 years of age, married ten years, was single when she gave birth to healthy twins. To prevent a recurrence she went to a hospital and had both tubes tied. She now would like to have another child and was told by a physician that an operation can be done to open the tubes and restore normal conditions. Her periods occur regularly but with much pain, which estrogens have not relieved. She also has spastic attacks of angina for relief of which injections of ½ grain (30 mg.) of morphine had to be used. I have not found an answer in any book, of which I have many.

M.D., Washington, D. C.

ANSWER.—Yes, the patency of the tubes may be restored by a surgical operation, thereby permitting normal intrauterine gestations. This case should be a favorable one for operation, because in all probability there is no infection in the tubes. However, after plastic operations on the tubes there is a relatively high incidence of tubal pregnancies.

PELVIC FRACTURE

To the Editor:—A severe pelvic fracture occurred involving all four pubic rami in a girl 6 years of age. The fractures are healing satisfactorily but are close to growth centers. Will future growth be disturbed so that the pelvic outlet may be distorted? It is important that this possibility be estimated accurately, as litigation is involved.

Ernest E. Myers, M.D., Lexington, Ky.

ANSWER.—As a rule, fractures of the pelvis even with some distortion do not cause dystocia. In this small child, if the fracture planes did not pass through the epiphysial areas probably growth disturbance will not result. Weight bearing and jumping, with severe jar of the pelvis, should be guarded against in the convalescence until complete bony union of the fracture is developed. Follow-up roentgenograms will show whether growth centers tend to close prematurely. Cesarean section may solve childbearing problems if they arise.

ACNE

To the Editor:—Is penicillin of value in acne simplex or acne vulgaris and, if so, which preparation and dosage are advisable?

M.D., New York.

ANSWER.—Penicillin apparently has no value in the treatment of simple acne. During the war it was given an extensive trial among service men in the South Pacific area who were incapacitated by severe acne, but with discouraging results.

VISUAL TESTS

To the Editor:—In *The Journal*, April 24, page 1118, the query of Dr. Joseph Bogan appears to have been misunderstood. The reference here, I believe, is to visual values as ordinarily expressed in the standard Snellen symbols and their equivalents denoted in the less conventional method as routinely employed, for instance, by the Naval examiner.

Answering the last part of the query first, to find the equivalent value of any Snellen notation in either method one has simply to determine the value of the unknown, or x. To illustrate:

$$20/25 = x/20$$
$$25x = 400$$
$$x = 16$$

Therefore 16/20 is the equivalent of 20/25. Conversely,

$$16/20 = 20/x$$
$$16x = 400$$
$$x = 25$$

Therefore 20/25 is the equivalent of 16/20. Proceeding in this manner, any equivalent value for a Snellen symbol as expressed in either method will naturally evolve. This will provide the information sought in the first part of Dr. Bogan's query.

It should be borne in mind, however, that this happy parallelism of visual values in the two methods does not go on indefinitely. Using 20 feet for the denominator of necessity restricts the scope of this method, inasmuch as one is now working with values contained within certain prescribed limits; that is, each is an integral unit of the whole, which, in this case, is 20 feet, or a total of 20 foot units (the range then being 20 to 1); hence, to go beyond 1/20 (equivalent 20/400) one would have to alter the original designation and revert to a unity the denominator of which is no longer 20 feet. Accordingly, it is clear that such a method of expressing visual values has its limitations, applying as it does to those persons who are capable of qualitative visual acuteness, and so in this sense is suitable only to a more or less selective group.

Finally, to answer the second part of Dr. Bogan's query, it will suffice to say that in the method using 20 feet for the numerator the test of vision is usually carried out with the examinee at the fixed distance of 20 feet from the chart. In the second method, the examinee approaches the test chart placed 20 feet away, and the distance from the chart when the 20 foot type read by the normal eye at this distance is seen becomes the numerator of the fraction indicating his visual acuity; to wit, 20/20, 12/20, 6/20 and so on to 1/20.

J. A. C. Gabriels, M.D., Albany, N. Y.